Chapter 4

Non-Traditional Pesticidally Active Compounds

Ahmed S. Abdel-Aty

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/ 46230

1. Introduction

Several organic compounds have not been approved as applied pesticides showed some useful actions against different pests. They may be considered as cores of new pesticides. Some compounds were prepared and assessed for their pesticidal activities. They showed persuasive effects as fungicides, herbicides (phytocidal effects), nematicides, molluscicides, insecticides as well as rodenticides comparing with commercial pesticides.

2. Materials and methods

2.1. Tested chemicals

Both indol-3-acetic acid GRG, El-Gomhouria Drug Company; indole-3-butyric acid, Sisco Research Laboratories, Mumbai, India, and other chemicals and solvents were purchased from El-Gomhouria Drug Company, Egypt. Standards of used herbicide, metribuzin (sencor), (4-amino-6-tert.butyl-4,5-dihydro-3-methylthio-1,2,4-triazin-5-one) and used fungicide metalaxyl, N-(2,6-dimethylphenyl-N-methoxyacetyl)-DL-alaninemethylester were donated by Kafr El-Zayat Company for pesticides, Egypt. Based on [1-2] with modification, some benzotriazole, benzylidine, coumarin, imidazolidine, indole, oxazolone and pyrazole, derivatives were prepared and identified [3-7].

2.2. Instruments

Structural confirmation was carried out by determination of melting points on kofler block; elemental micro analysis (C, H, N, X); IR, UV, NMR and Mass spectroscopy measurements in Microanalytical Center, Cairo University, Giza, Egypt. NMR spectra were recorded on Varian Mercury-VX-300 NMR Spectrometer using tetramethylsilane (TMS) as a standard. Mass spectra were recorded on a Schimadzu MS5988-mass spectrometer at 70 ev. Determination of soluble sugars, chlorophyll contents and total soluble phenols (TSP) were done on Unico-1200 Spectrophotometer. Both enzymatic activity and nucleic acids

contents were measured using Nicolet 100 UV-VIS Spectrophotometer, Thermo Electron Corporation.

2.3. Tested fungi

Wood decay fungi, *Coriolus versicolor* (Linnaeus) Quélet, strain CTB 863 and *Gloeophyllum tarbeum* (Persoo ex Fries) Murrill, strain BAM Ebw. 109 were provided from Laboratory of Wood Technology, Ghent University, Belgium. *Alternaria alternata*, *Fusarium calmorum*, *F. oxysporum*, *Helmintho-sporium* sp, *Macroformina phaseoli*, *Pythium debarianum*, and *Rhizoctonia solani* were provided by Plant Pathology Department, Faculty of Agriculture, Alexandria University, Egypt.

2.4. Tested animals

Albino norway rats strain (*Rattus norvegicus* var. *albus*) were taken from the Laboratory of Rodents, Department of Pesticide Chemistry and Technology, Faculty of Agriculture, Alexandria University, Egypt. *Spodoptera littoralis* Boisd strain was grown in the breeding sector of Pesticide Chemistry Department, Faculty of agriculture, Alexandria University, Egypt. *Thepa pisana* and *Eobania vermiculata* Muller snails, family Heliecidae were collected from gardens of Faculty of Agriculture, Alexandria University.

Through these studies, *In vitro* antifungal assessment of the tested compounds was conducted using a mycelial radial growth technique [8-9]. Inhibition percent and IC_{50} (the concentration caused 50% inhibition) values of the hyphal growth were calculated [10-11]. Significance was elucidated through three-way ANOVA completely randomized Student-Newman-Keuls Test. *In vivo* determination of polyphenoloxidase [12], Peroxidase [13] activities and DNA and RNA contents [14] were conducted. Protein content (mg) [15] and the specific activities of all treatments were calculated. Insecticidal activity was tested on both the 4^{th} and 6^{th} larval instars of *S. littoralis* Boisd. The tested larvae were reared on a semi artificial growing medium [16-17]. Mortality percents were calculated.

Seed treatment was carried out according to [18]. Toxic effects on the seedling stage (after germination) of both root and shoot systems using the plain agar was done according to [19]. In dried wheat seedlings, total soluble sugars (T.S.S), reducing sugars (R.S) and non-reducing sugars (non-R.S) expressed as μg/g dried plant were determined [20]. Chlorophyll (a and b) contents were calculated in μg/g tissue fresh weight [21]. Total soluble phenolics were determined as mg gallic acid equivalent (mg GAE)/g fresh weight [22-23]. Mortality test was carried out on Albino norway rats strain (*Rattus norvegicus* var. *albus*) by (No-choice test) [24]. Haemoglobin concentration (Hb%) was determined according to [25], using Boehring Mannhein Gm bH Diagonestic Kit. Haematocrit value (Hc%), white blood cells (WBCs) and red blood cells (RBCs) were counted [26]. *In vivo* determination of alanine transaminase (sALT) and aspartate transaminase (sAST) activities were carried out based on [27] using Boehringer Mannhein Gm bH Diagonestic Kits. Effects of the prepared compounds could be summarized in the following points:

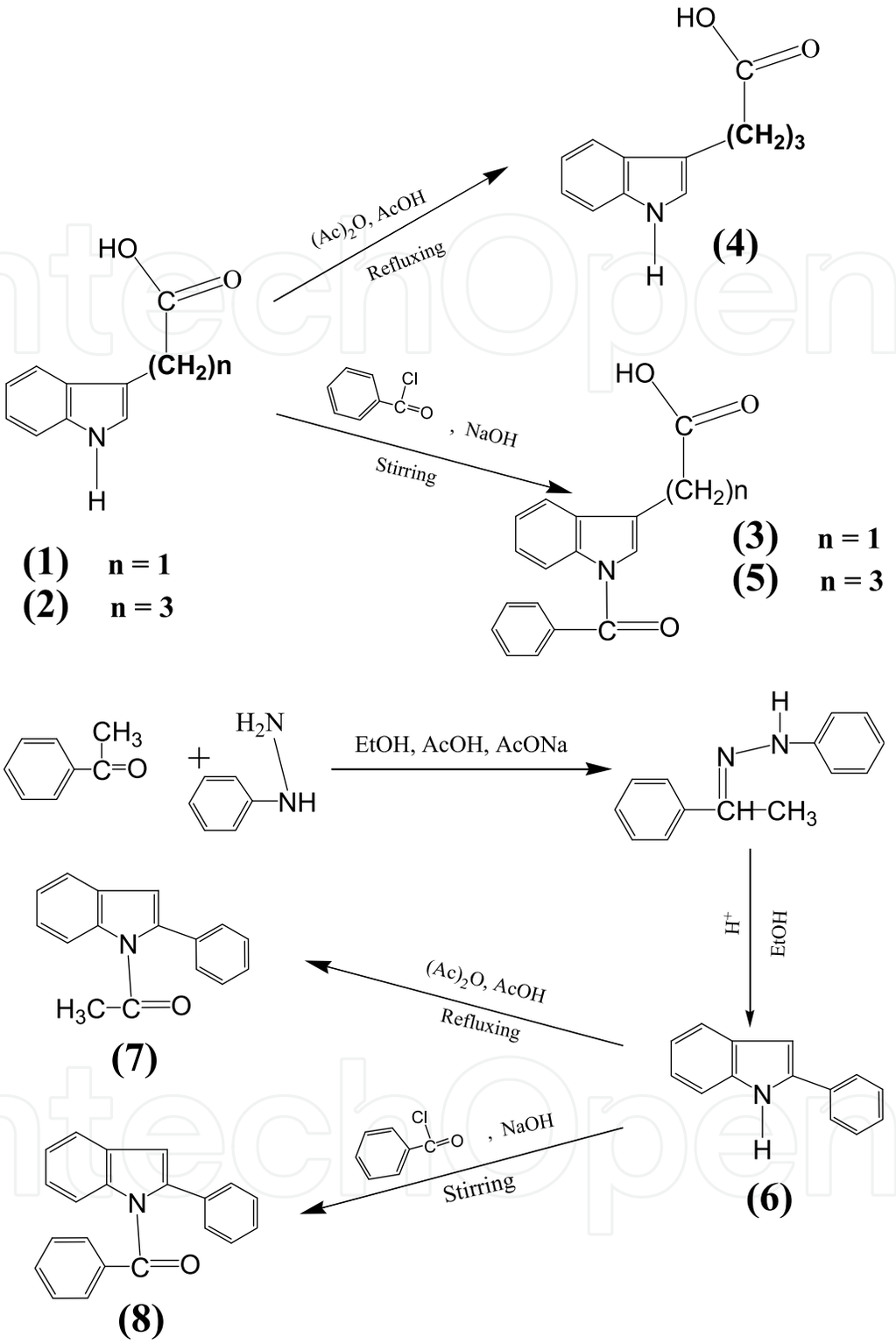
3. Results and discussion

3.1. Fungicidal activity of some indole derivatives [7]

In the vast heterocyclic structural space, the indole nucleus occupies a position of major importance as antimicrobial agents. Combination of IAA (at 100 μg/ml) with *Cryptococcus laurentii* suppressed blue and gray mold infections on pear fruit more than *C. laurentii* alone [28]. It exhibited antifungal activity against *Gibberella pulicaris* suppressing the dry rot infection of wounded potatoes optimally when combined with phenylacetic acid and tyrosol [29]. Its 5-methoxy- derivative and 1H-indole-4,7-diones showed antifungal and antibacterial activities against several species [30-31]. So, besides, both indol-3-acetic acid and indol-3-butyric acid, purchased from El-Gomhouria Drug Company, Egypt, Six indole derivatives: 1-benzoyl indole-3-acetic acid, 1-acetylindole-3-butyric acid, 1-benzoylindole-3-butyric acid, 2-phenylindole, 1-acetyl-2-phenylindole and 1-benzoyl-2-phenylindole were prepared and structurally confirmed. Their fungicidal effects against the damping off fungi as a very important economical group threating several crops like *Fusarium calmorum, Rhizoctonia solani, Pythium debarianum* and *Macrofomina phasoli* that causes post harvest fruits rotting were compared with the technical grade of metalaxyl (Radomil). As shown in Table (**1**), against *F. calmorum*, derivatives of 2-phenylindole were more effective than the standard fungicide. 1-Acetylindole-3-butyric acid appeared the most active. The other derivatives were less effective than metalaxyl. *M. phaseoli* was affected with less toxicity degree. 1-Benzoyl-2-phenylindole slackened in its effect to less than the standard. Fungicidal activity was increased against *P. debarianum* in all cases in comparison to *F. calmorum*. 2-Phenylindole, 1-acetyl-2-phenylindole and 1-benzoyl-2-phenylindole inhibited its hyphal growth with IC_{50} values equaled 17.7, 15 and 81 μg/ml, respectively in comparison to 211 μg/ml of the standard fungicide. 1-Acetylindole-3-butyric acid was very active with IC_{50} value equaled 19 μg/ml. *R. solani* appeared tolerant than other fungi for all compounds including the standard. From the mentioned results, fungicidal activity proved to be a function of both treated fungus and the structure. *P. debarianum* was the most sensitive, followed by *F. calmorum*, *R. solani* and *M. phaseoli.* Their hyphal growth was inhibited with Mean ± SE equaled 35.52 ± 2.16, 30.02 ± 1.99, 28.02 ± 1.66 and 25.31 ± 1.49 μg/ml, respectively with significant differences. Regarding the structure activity relationship, acylation of the natural auxin enhanced its fungicidal activity. Substitution with a 1-benzoyl moiety in indole-3-acetic acid (IAA) slightly increased the activity although in case of indole-3-butyric acid (IBA) it showed no significant effect. Acetylation of IBA strongly multiplied the activity against all tested fungi. Replacing the 3-aliphatic chain with 2-phenyl moiety firmly improved the toxicity against all the treated fungi. While benzoylation of 2-phenylindole decreased its activity, acetylation maintained its toxicity high. Based on statistical analysis, 1-acetylindole-3-butyric acid, 2-phenylindole, 1-acetyl-2-phenylindole and 1-benzoyl-2-phenylindole exhibited their inhibition with Mean ± SE equaled 44.65 ± 3.91, 43.07 ± 3.32, 42.36 ± 3.38 and 31.02 ± 2.76 μg/ml, respectively surpassing the standard fungicide with 29.05 ± 2.46 μg/ml. The other structures were less effective than the standard fungicide. The effect on hypha growth agreed with [32] who referred the reduction of mycelial dry weight and protein content of *F. oxysporum lycopersici* to IAA. It also inhibited *M. phaseolina* mycelial growth *in vitro* and reduced

the charcoal rot disease both in field and greenhouse [33]. Polyphenoloxidase in *R. solani* systematically responded to 2-phenylindole with IC_{50} equaled 80.27 μg/ml. 1-Acetylindole-3-butyric acid inhibited it with 39% at the lowest concentration, followed by activation with 78.9 and 84% of control at 1.0 and 2.0 IC_{50} values, respectively. 1-Acetylindole-3-butyric acid was more effective than 2-phenylindole inhibiting it with 41.5 and 80.2 μg/ml IC_{50} values comparing with 87.6 and 117.2 μg/ml, respectively in case of *F. calmorum* and *M. phaseoli*. While *P. debarianum* enzyme activity was inhibited by 1-acetylindole-3-butyric acid with IC_{50} equaled 45.6 μg/ml, 2-phenylindole enhanced it with activating concentration of 50% (AC_{50}) equaled 35.1 μg/ml. Regarding peroxidase, in *R. solani* it was activated with AC_{50} equaled 14.5 and <11.7 μg/ml in case of 2-phenylindole and 1-acetylindole-3-butyric acid, respectively**.** Both the two compounds exhibited narrow ranged inhibitory effects against the enzyme from *P. debarianum*. While in *M. phaseoli* treatment, the enzyme was activated systematically with 1-acetyl indole-3-butyric acid with AC_{50} < 5.9 μg/ml, 2-phenylindole affected it from -39 to 54.3 % inhibition regularly with increasing its concentration. It affected the activity of *F. calmorum* enzyme from 85.0 to -115.3 % inhibitions within its concentration range. This activity was inhibited with 2-phenylindole with IC_{50} equaled 49.9 μg/ml. On the other sight, both RNA and DNA contents were affected. Both RNA and DNA molecules are related to each other, so the results obtained were exhibited in systematic response. In *F. calmorum*, RNA and DNA contents as compared with control (51.5 and 49.5 mg/liter) were found to be reduced at the tested IC_{50} rates of 2-phenylindole. This reduction was increased with increasing the tested concentration to 0.5 IC_{50} then RNA content was dramatically increased to 26.3 and 24.7 mg/liter and DNA content was increased to 25.3 and 23.8 mg/liter at 1 and 2 IC_{50}. RNA and DNA contents in *R. solani* highly increased and reached to the maximum peak of increase at 1.0 IC_{50} of 2-phenylindole. RNA and DNA contents in *M. phasoli* were reduced to less than 50% of control at the tested rates. They changed from 8.3 to 5.9 and from 8.0 to 5.7 mg/liter comparing with 16.1 and 15.5 mg/liter of control. These contents of *P. deparianum* behaved the same trend of these in *M. phasoli* changing from 30.6 to 11.4 and from 29.4 to 10.9 mg/liter comparing with 32.2 and 31 mg/liter of control.

1-Acetylindole-3-butyric acid affected both RNA and DNA contents differently according to the tested fungus and concentration. It reduced them in *F. calmorum* in systematic arrangement at all the tested IC_{50} rates comparing with control. While RNA and DNA contents in *M. phasoli* were decreased by increasing the tested rate with systematical arrangement. This decreasing effect was noticed in all fungi. Their contents were reduced from 45.4 to 20.3 and 43.6 to 19.5 mg/L in case of *F. calmorum*, they were reduced from 12.9 to 6.7 and from 11.7 to 6.5 in case of *M. phaseoli* comparing with 51.5, 49.5, 16.1 and 15.5 of their control, respectively. While the contents from *P. debarianum* were decreased untill 0.5 IC_{50} and increased again at the two highest concentration rates**,** they were systematically increased with increasing the concentration in case of *R. solani.* General descriptive analysis proved that 2-phenylindole affected *M. phasoli* significantly greater than *P. debarianum* with



1 Indole-3-acetic acid
2 Indole-3-butyric acid
3 1-Benzoyl indole-3-acetic acid
4 1-Acetyl indole-3-butyric acid
5 1-Benzoyl indole-3-butyric acid
6 2-Phenylindole
7 1-Acetyl-2-phenylindole
8 1-Benzoyl-2-phenylindole

Scheme 1. Preparation of Compounds 1-8

Treated fungus	Treatment	IC_{50} (95%C L) µg/ml	Slope ± S.E	χ^2	TF
F. calmorum	Indole-3-acetic acid [d *]	420 (222 – 823)	0.6 ± 0.005	4.75	2.19
	1-Benzoyl indole-3-acetic acid [c]	523 (322 – 859)	0.87 ± 0.011	7.04	2.72
	Indole-3-butyric acid [a]	576 (388 – 858)	1.28 ± 0.025	2.78	3.00
	1-Acetyl indole-3-butyric acid [i]	26.6 (21.3 –33.3)	1.41 ± 0.01	4.54	0.14
	1-Benzoyl indole-3-butyric acid [b]	513 (335 – 793)	1.03 ± 0.015	1.29	2.67
	2-Phenylindole [h]	67.4 (53.0- 85.8)	1.11 ± 0.008	8.57	0.35
	1-Acetyl-2-phenylindole [g]	86.7 (66.4 – 113)	0.98 ± 0.007	5.33	0.45
	1-Benzoyl-2-phenylindole [f]	99.9 (77 – 129.9)	1.02 ± 0.008	0.63	0.52
	Metalaxyl [e]	192 (126 – 296)	0.69 ± 0.006	3.6	1.0
M. phaseoli	Indole-3-acetic acid [a]	807 (440 – 1514)	0.81 ± 0.011	2.83	4.66
	1-Benzoyl indole-3-acetic acid [d]	572 (359 – 923)	0.97 ± 0.014	2.99	3.30
	Indole-3-butyric acid [b]	699 (458 – 1073)	1.38 ± 0.003	1.28	4.03
	1-Acetyl indole-3-butyric acid [f]	59.0 (47.0 – 74)	1.21 ± 0.009	3.87	0.34
	1-Benzoyl indole-3-butyric acid [c]	448 (325 – 622)	1.38 ± 0.026	2.62	2.59
	2-Phenylindole [i]	96 (74.6- 123.4)	1.06 ± 0.008	8.1	0.55
	1-Acetyl-2-phenylindole [h]	93 (71.7 – 120.0)	1.03 ± 0.008	7.78	0.54
	1-Benzoyl-2-phenylindole [g]	355 (247 – 514)	1.02 ± 0.001	2.18	2.05
	Metalaxyl [e]	173 (127 –237.6)	0.93 ± 0.008	4.78	1.00
P. debarianum	Indole-3-acetic acid [b]	301 (207.9- 438)	0.93 ± 0.001	3.76	1.43
	1-Benzoyl indole-3-acetic acid [b]	171 (125 – 236)	0.91 ± 0.008	3.96	0.81
	Indole-3-butyric acid [d]	249 (179 – 349)	0.98 ± 0.001	9.33	1.18
	1-Acetyl indole-3-butyric acid [g]	19 (14.4 – 24.8)	1.1 ± 0.006	1.72	0.09
	1-Benzoyl indole-3-butyric acid [a]	488.4 (319 –753)	1.0 ± 0.14	0.46	2.31
	2-Phenylindole [f]	17.7 (11.8 –26.4)	0.67± 0..004	0.48	0.08
	1-Acetyl-2-phenylindole [g]	15.0 (9.5 – 23.2)	0.61 ± 0.004	2.15	0.07
	1-Benzoyl-2-phenylindole [e]	81 (57.2 – 115)	0.73 ±0.005	3.99	0.38
	Metalaxyl [c]	211 (145 – 310)	0.80 ± 0.007	1.03	1.00
R. solani	Indole-3-acetic acid [c]	1009 (539–1923)	0.94 ±0.016	4.42	4.36
	1-Benzoyl indole-3-acetic acid [c]	1244 (633–2515)	0.71 ± 0.008	9.08	5.38
	Indole-3-butyric acid [a]	644 (368 – 1151)	0.79 ± 0.01	2.38	2.78
	1-Acetyl indole-3-butyric acid [i]	117 (97.6 – 141)	1.57 ± 0.018	6.1	0.51
	1-Benzoyl indole-3-butyric acid [b]	663 (377 – 1192)	0.79 ± 0.01	2.64	2.87
	2-Phenylindole [h]	34.6 (25.1 –47.5)	0.81 ± 0.005	7.14	0.15
	1-Acetyl-2-phenylindole [f]	37.5 (27.6 –50.7)	0.85 ± 0.005	1.79	0.16
	1-Benzoyl-2-phenylindole [d]	122.2 (93 –161)	1.0 ±0.008	3.31	0.53
	Metalaxyl [e]	231 (167.7 –321)	0.98 ± 0.01	3.21	1.00

TF: Toxicity factor related to Metalaxyl * Significance at 0.05 level against each fungus DF = 4

Table 1. *In Vitro* fungicidal activity of indole derivatives

(8.42 ± 0.86 and 25.05 ± 1.84) and (8.08 ± 0.83 and 24.1 ±1.78) mg/liter means ± SE of RNA and DNA contents. Although there was no significant difference between *R. solani* and *F. calmorum*, they differed significantly from the other tested fungi with (29.2 ± 2.55 and 29.23 ± 0.55) and (28.12 ± 2.45 and 28.16 ± 0.42) mg/liter of RNA and DNA contents. The same arrangement was exhibited in treatment with 1-acetylindole-3-butyric acid except achieving a significant difference among all the tested fungi. RNA contents were 10.57 ± 0.78, 23.01 ± 1.61, 28.57 ± 1.07 and 34.31 ± 2.61 mg/liter, while DNA contents were 10.09 ± 0.73, 22.07 ± 1.53, 27.52 ± 1.01 and 33.0 ± 2.51 mg/liter in case of *M. phasoli*, *P. debarianum*¸ *R. solani* and *F. calmorum*, respectively. Comparing with the untreated fungus, all sugar types in *M. phasoli* were reduced at 2-phenylindole concentrations with non-systematic arrangement. *R. solani* sugars contents were strongly multiplied at 0.1 and 0.25 IC_{50} concentrations, followed by a firm decrease at 0.5 IC_{50} and this reduction was increased at 1.0 IC_{50}. This effect was differed from the effect of 1-acetylindole-3-butyric acid as both reduced and non-reduced sugars were systematically decreased with increasing the concentration. Reduced, non-reduced and total soluble sugars were *in vivo* affected with the two studied compounds in a treated fungus and concentration dependent effect.

It could be concluded that 2-phenylindole and 1-acetylindole-3-butyric acid affected both RNA and DNA contents in the tested fungi, which may develop deformed and dead cells. These effects of indole acetic acid and some derivatives are due to formation of 3-methylene-2-oxindole, which may conjugate with DNA bases and protein thiols [34]. There were highly effective against polyphenoloxidase and peroxidase activities that means disturbance in the cell physiology as [28] revealed that IAA alone or with *C. laurentii* stimulated catalase, peroxidase and polyphenol oxidase activities of pear fruit. The studied indole derivatives may affect the treated fungi in another site of action as [35] found that IAA and IBA greatly increase somatic segregation in *Aspergillus nidulans* and increasing their concentrations increased mitotic segregation of the fungus.

3.2. Insecticidal activity of the prepared indole derivatives [36]

The Egyptian cotton leaf-worm, *S. littoralis* (Boisd.) is an important polyphagous insect attacking several crops and ornamentals worldwide. Persuasive effects against it were referred to plant alkaloids [37-39]. So, this study aimed to examine the indole derivatives against its stages.

Lethal effects

The tested compounds were more effective against the 4th larval instar than the 6th instar after 5 days except 1-acetylindole-3-butyric acid (**3**) and 1-acetyl-2-phenylindole (**7**). The effect was increased after nine days in all cases. 1-Benzoyl-2-phenylindole (**8**) was less effective on the 6th instar. 2-Phenyl indole (**6**) and its 1-acetyl derivative (**7**) were more effective on the 6th instar. Lethal effects were increased in all tested compounds against 6th instar except for compounds **2** and **5**. It was also found that substitution of compound **3** raised the toxicity on the 6th instar. The increase due to its acetylation was greater than

benzoylation. Substitution of 2-phenyl moiety on the indole ring in stead of side aliphatic carboxylic group increased the larval mortality in case of compound **6** more than in indole-3-acetic acid (**1**). Substitution with 1-acetyl on 2-phenylindole multiplied the lethality against the two tested larval instars, while substitution with 1-benzoyl in compound **8** enhanced the toxicity only against the 4th larval instar. The most effective compound was indole-3-butyric acid (**2**) with 70.9 and 39.7 μg/gm LC_{50} values on the 4th instar after 9 and 13 days, while 1-acetylindole-3-butyric acid **(3)** and 1-acetyl-2-phenylindole (**7**) were more effective with 151.4 and 80.6 μg/gm LC_{50} values against the 6th instar. So**,** compounds **2, 3** and **7** were chosen for egg treatment.

Sub-lethal effects (Fresh body weight)

The larval weight of the 4th instar (after 7 days) was differently affected with the applied derivatives. Benzoylation of indole-3-acetic acid in compound **4** affected the larval weight in non systematic arrangement with concentrations. Acetylation of indole-3-butyric acid in compound **3** reduced the larval weight at 50 and 100 μg/gm, followed by an increase at higher concentrations. On the contrary, its benzoyl derivative (compound **5)** increased the larval weight at lower concentration, followed by reduction at the two higher concentrations. Light reduction occurred at low concentrations, followed by gradual activation with increasing the concentration, which was exhibited by compound **6**. Substitution with 1-acetyl moiety in compound **7** increased the larval weight at low concentration followed by inhibition percents ranging from 3.2 to 18.5% of control at 100-1000 μg/gm. Benzoylation of 2-phenylindole in compound **8** decreased the reduction effect more than compound **7**. Comparing with the untreated 6th larval weight (0.77 gm) after two days, all the tested compounds reduced the treated larval weight at all concentrations with different degrees and arrested their development to 7 days after treatment. Compounds **1** and **2** showed narrow differences among their concentrations with less reducing effect, followed by compounds **8, 6**, **5** and **7**. Compounds **3** and **4** were the most active derivatives in weight reduction. From these results, the hormonal effect was obviously clear through the activation of larval weight in most cases when applied earlier at the 4th instar more than at the 6th instar (Figure **1**).

Development

Untrated 4th instar larvae developed to pupal and adult stages after 6-7 and 9-10 days, respectively. Indole-3-acetic acid (**1**) at 10 μg/gm delayed this development to 29 and 45 days, respectively. However, the other compounds were less effective causing developing of 50, 10, 75, 92, 13, 63, and 83% of the treated larvae to pupae in case of compounds **2**, **3**, **4**, **5**, **6**, **7** and **8**, respectively after 21 days. While, compounds **5** and **7** caused complete transformation of the treated population to adults, compounds **2**, **4**, **6** and **8** caused developing of 75, 75, 55 and 67 % of pupae to adults. Compound **3** (1-acetylindole-3-butyric acid) was the most effective structure blocking adult emergence to 25% of the treated population after 45 days. Regarding 6th larval instar, its control completely developed to the pupal and adult stages after 2-3 and 7-8 days, respectively. All compounds arrested the

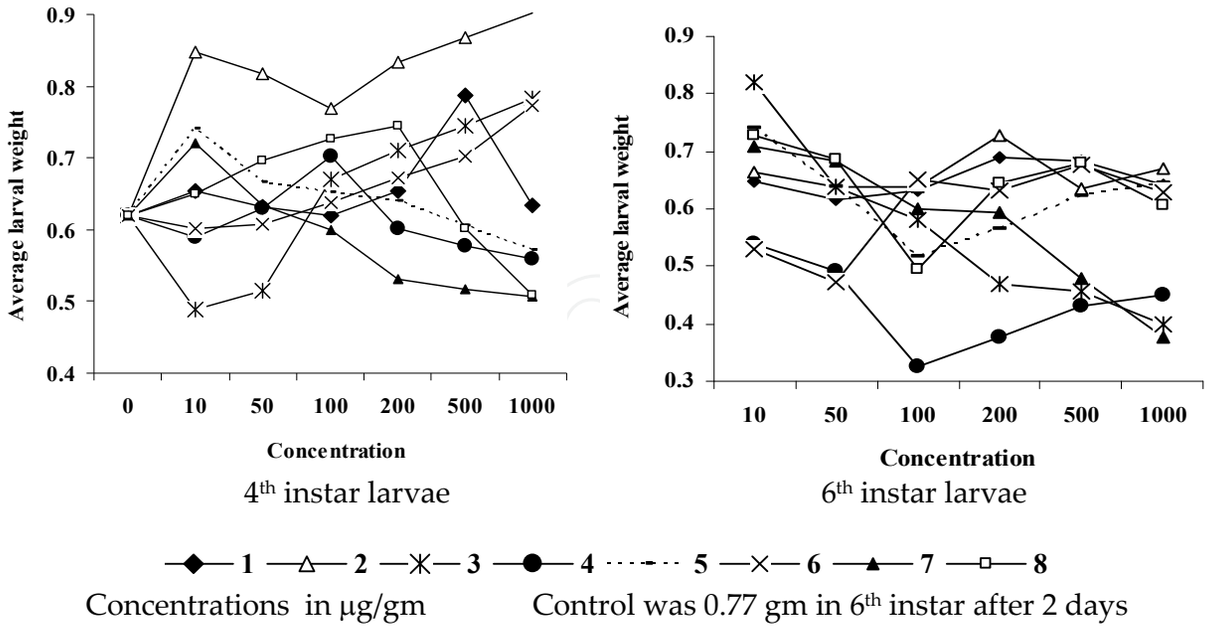


Figure 1. Effect of the tested compounds on fresh larval weight of *S. littoralis*; shown as average weight (gm) after 7 days of treatment. **1:** Indole-3-acetic acid; **2:** Indol-3-butyric acid; **3:** 1-Acetylindole-3-butyric acid; **4:** 1-Benzoylindole-3-acetic acid; **5:** 1-Benzoylindole-3-butyric acid; **6:** 2-Phenylindole; **7:** 1-Acetyl-2-phenyl indole; **8:** 1-Benzoyl-2-phenyl indole

larval development except compounds **3** and **5,** which caused 25 and 18% pupation after 13 days. Compound **1** was the most effective inhibiting the adult emergence, followed by compound (**4**), 1-benzoylindole-3-butyric acid (**5**), indole-3-butyric acid (**2**), 2-phenylindole (**6**), 1-acetylindole-3-butyric acid (**3**), 1-benzoyl-2-phenylindole (**8**) and 1-acetyl-2-phenylindole (**7**). They blocked the adult emergence to 7, 14, 31, 33, 39, 46, 48 and 50% of the treated population after 35 days. From the results, the duration of *S. littoralis* larval stage was significantly affected. It required a longer time to reach next stadium differing from control (Figure **2**).

Malformations

Comparing with the untreated larvae, compounds **1** and **2** exhibited 14.6% and 16.7% malformation in the intermediates of the treated 4th larval instar at 200 µg/ml, with no effect on 6th larvae. Acetylation of indole-3-butyric acid in compound **3** affected the intermediates at lower concentrations in the 6th larval instar, while its benzoylation increased this effect against the 4th instar only. Acetylation of 2- phenylindole caused 32.6 and 61.1% intermediate malformation at 100 and 200 µg/ml in treated 4th instar larvae. 1-Benzoyl-2-phenylindole affected 4th larvae at 10 µg/ml with 7.6% malformation. However, its effect was as high as 10.1% at the higher concentrations against 6th instar intermediates. These malformation symptoms appeared as larval-pupal intermediates in which the posterior portion of the body only exhibited the pupal shape, while the anterior portion had larval head capsule and thoracic legs (Figure **3**). Malformation of the produced pupa (forming abnormal pupa without wings or that failed to shed the larval cuticle) resulted from the 4th

larval instar, which was more sensitive than that from 6th larval instar to treatment with compounds **1-3**, 2-phenylindole (**6**) and 1-benzoyl-2-phenylindole (**8**). The effects of compounds **4** and **5** depended on the applied concentration. Benzoylation of 2-phenylindole increased the pupae malformation. Adult malformation (adult failed to shed the pupal cuticle or adult with dwarf wings) was affected with the tested compounds, concentration and larval instar. Adult emergence from both treated instars was affected. Compounds **1**, **2**, **3** and **5** blocked the adult emergence to 10.3 - 47.4%, 16.7 - 50%, 20.2 - 50.6% and 10.6 - 55.7% in systematic arrangement, respectively from 4th larval populations comparing with 100% of control. The blocking effect was reduced with increasing the concentration. They blocked adult emergence to 25.9-43.7%, 36.8-57.0%, 31.9-40.9% and 32.5-66.9%, respectively in non systematic arrangement in case of the 6th larval population. Compound **4** caused 9.5-20.8% and 22.9-69.5% adult emergence in case of the treated 4th and 6th larval instars, respectively. Although 2-phenylindole and its 1-acetyl derivative affected the adult emergence from both treated instars in non systematic arrangement, its 1-benzoyl derivative blocked the adult emergence with increasing the concentration. Adult emergence was more inhibited from 4th larval instar treatment indicating that treatment of the lower larval instars gave good results of control (Figure **4**).

Effect on eggs

Egg hatchability was inhibited increasingly in systematic arrangement with concentrations. Both 1-acetylindole-3-butyric acid (**3**) and 1-acetyl-2-phenyl-indole (**7**) completely stopped hatching when mixed at 100 μg/gm with the medium. As the untreated egg mass hatched completely within 24 hours, treated eggs took 48-96 hours and 6-7 days at high concentrations of compound **2** and compounds **3** & **7,** respectively. After 48 hours, only dipping the egg masses in solutions of compound **2** inhibited hatching with IC_{50} value equaled 29.1 μg/ml and killed the produced larvae with LC_{50} value equaled 26.2 μg/ml. Transferring treated eggs to the poisoned medium enhanced the toxicity to IC_{50} equaled 13.2 μg/gm and LC_{50} equaled 15.2 μg/gm. Although acetylation of compound **3** decreased larval mortality in dipping technique with or without transferring the eggs to the poisoned medium, it enhanced egg-hatching inhibition when dipped only in the toxic solutions. Although compound **7** was less effective when egg masses were dipped in it, its mixing with the used medium greatly enhanced the effect with IC_{50} value equaled 15.3 μg/gm on egg-hatching and LC_{50} value equaled 7.5 μg/gm on larval mortality. In conclusion, mortality of 4th instar larvae was increased with increasing the aliphatic side chain. Substitution of N-H of 2-phenylindole raised the toxicity, vice versa in case of indole-3-butyric acid against the same instar. The tested compounds affected larval weight, pupation and adult emergence indicating that treatment induced an effect typical to juvenile hormone excess. These effects varied according to the tested compound. These delayed effects are expressed as developmental abnormalities in the adult stage. These effects may be due to oxidative decarboxylation forming 3-methylene-2-oxindole, which may conjugate with DNA bases and protein thiols [34]. It may be also due to inhibition of

cholinesterase [40]. Its effect is associated with cell phenoloxidase (PO) and peroxidase activities [6, 41]. Phenoloxidase (PO) is believed to be a key mediator of immune function in insects.

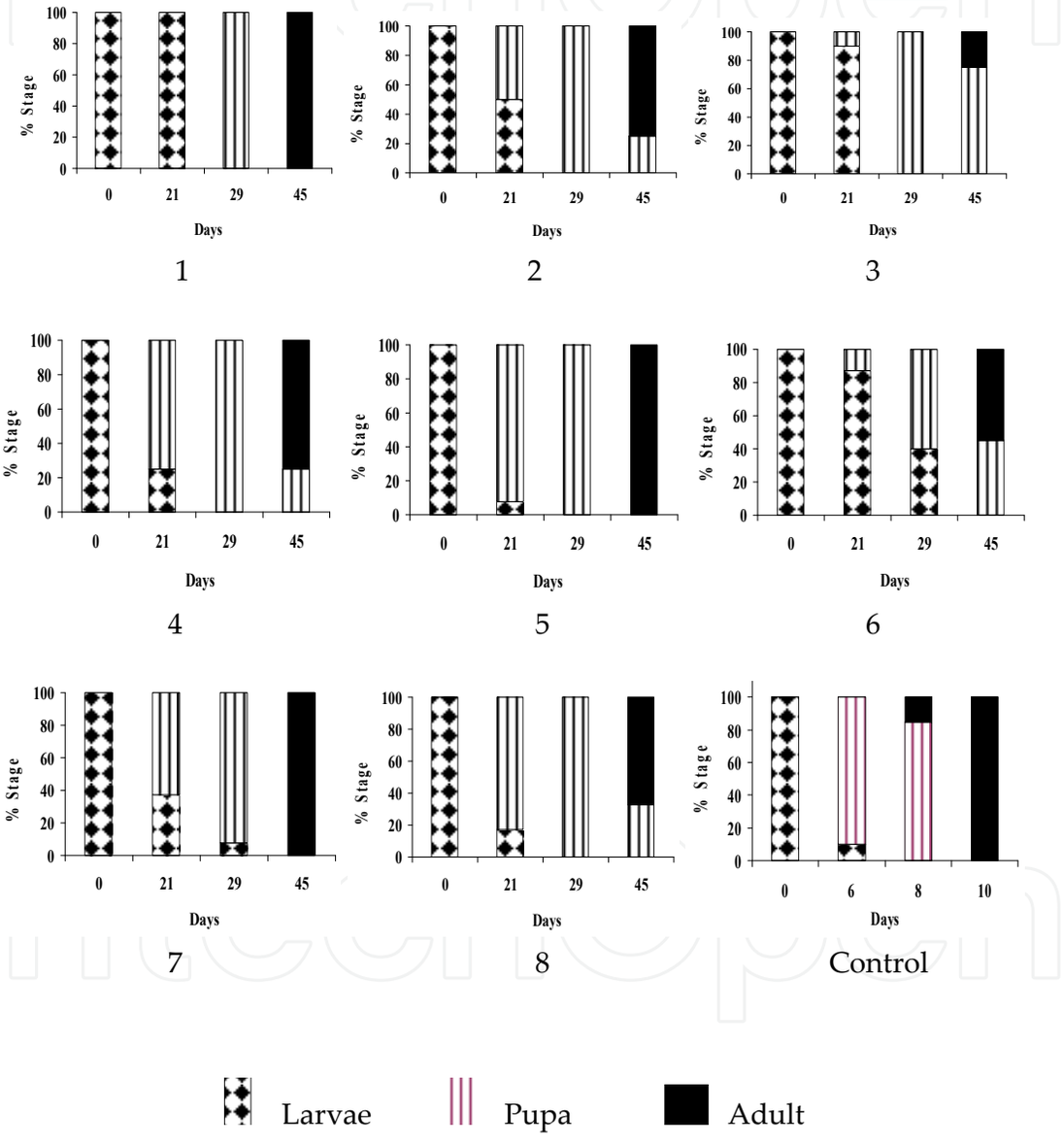
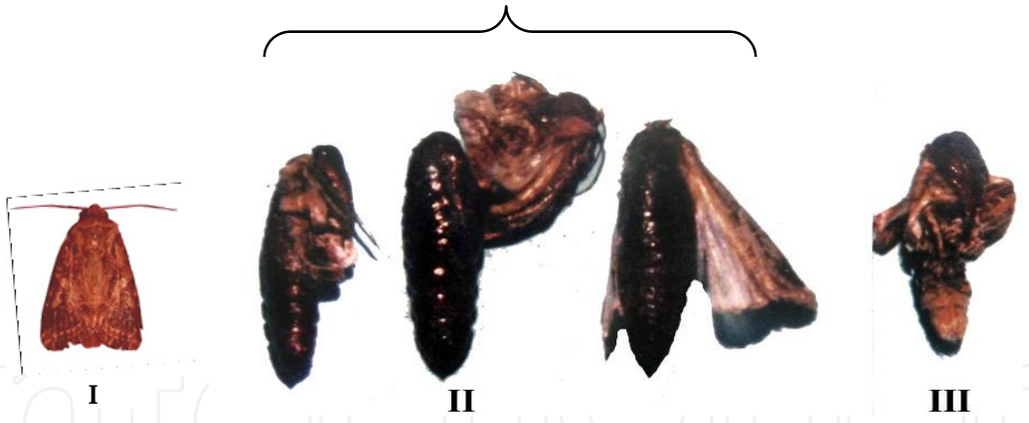


Figure 2. Effect on *S. littoralis* 4th larval development at 10 μg/gm; **1:** Indole-3-acetic acid; **2:** Indol-3-butyric acid; **3:** 1-Acetylindole-3-butyric acid; **4:** 1-Benzoylindole-3-acetic acid; **5:** 1-Benzoylindole-3-butyric acid; **6:** 2-Phenylindole; **7:** 1-Acetyl-2-phenyl indole; **8:** 1-Benzoyl-2-phenyl indole

Malformations in the prod uced pupae comparing with control

I Normal pupa (control), **II,** juvenilized larval-pupal intermediates, **III,** abnormal pupae failed to shed the larval cuticle



Different abnormal forms of the produced adults comparing with control

I, Normal adult (control), **II,** abnormal adults failed to shed the cuticle, **III, a**dult with dwarf wings

Figure 3. Maleformations effects of the tested indole derivatives

This notice may clarify the effect of the tested compounds on adult emergence and pupation. N-H and N-substituted indole-2- and 3-carboxamide showed a strong inhibitory (95-100%) effect on superoxide anion (SOD). Substitution on 1-position of the indole ring caused significant differences between the activity results regarding lipid peroxidation inhibition [42] emphasizing the differences in effects due to the derivative structure.

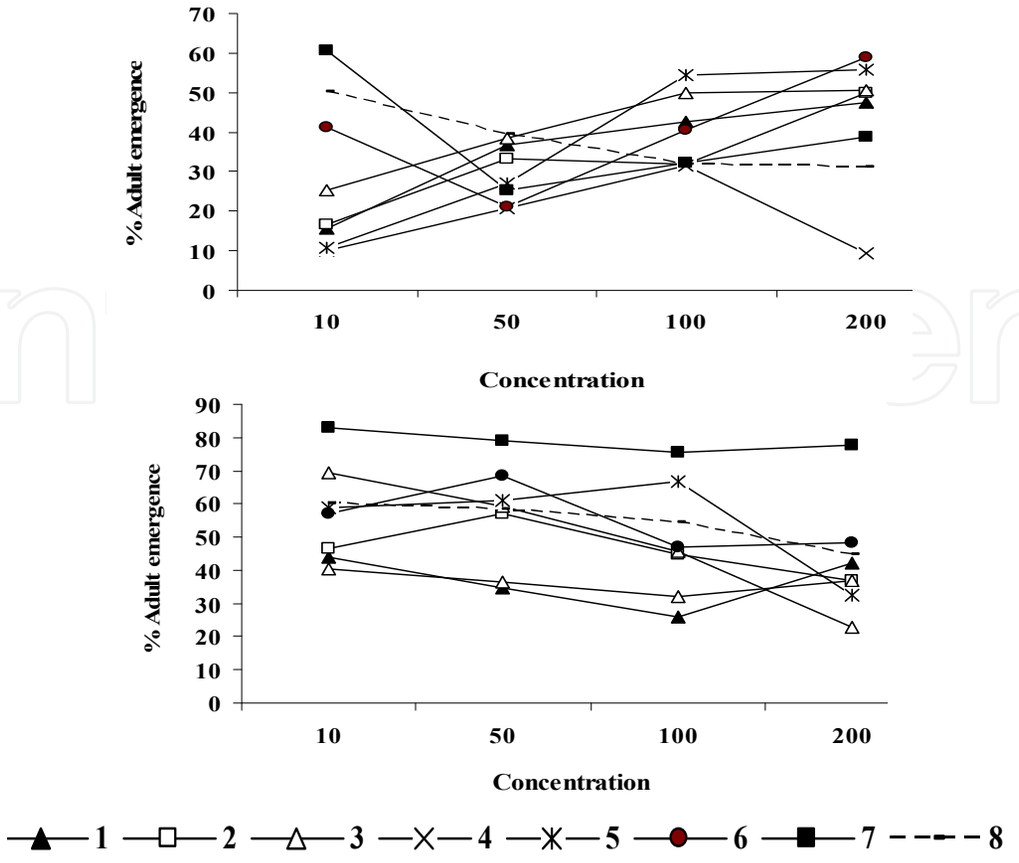
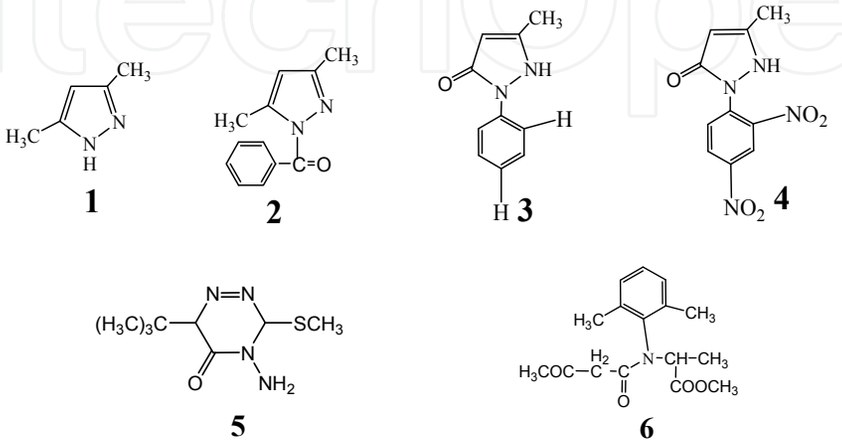


Figure 4. Emergence percents of *S. littoralis* adults produced from treated larvae. **Upper,** from treated 4th instar**; Lower,** from treated 6th larval instar**;** Concentrations (µg/gm). **1:** Indole-3-acetic acid; **2:** Indol-3-butyric acid; **3:** 1-Acetylindole-3-butyric acid; **4:** 1-Benzoylindole-3-acetic acid; **5:** 1-Benzoylindole-3-butyric acid; **6:** 2-Phenylindole; **7:** 1-Acetyl-2-phenyl indole; **8:** 1-Benzoyl-2-phenyl indole

3.3. Pesticidal activities of some pyrazole derivatives [5]

Due to antimicrobial activity of some 3,5-dimethylpyrazole derivatives [43], 3,5-dimethylpyrazole (**1**), 1-Benzoyl-3,5-dimethylpyrazole (**2**), 3-methyl-1-phenylpyrazol-5-one (**3**) and 3-methyl-1-(2,4-dinitrophenyl)-pyrazol-5-one (**4**) were prepared, structurally confirmed and studied for their effects against *Fusarium oxysporum*; *Pythium debarianum Rhizoctonia solani* and *Macrofomina phaseoli*. Metalaxyl (Radomil), methyl- N-(2,6-dimethylphenyl-N-methoxyacetyl)-DL-alaninate (**6**) was used as a standard fungicide. Their phytocidal effects were determined on both wheat (*Triticum aestivum*) and squash (*Cucurbita pepo*) seedlings comparing with metribuzin (sencor), 4-amino-6-tert.butyl-4,5-dihydro-3-methylthio-1,2,4-triazin-5-one (**5**). Insecticidal effects were evaluated on the 4th instar of cotton leaf worm, *S. littoralis* Boisid. Their fungitoxic effects as IC_{50} values illustrated that comparing with metalaxyl, *R. solani* was less affected than the other fungi. 3,5-Dimethylpyrazole (**1**) proved to be moderately toxic with470, 380 and 330 µg/ml IC_{50} values against *P. debarianum*, *F. calmorum* and *M. phaseoli*, respectively after 6 days exposure, whereas 1-benzoyl-3,5-dimethylpyrazole (**2**) reduced the activity against all the tested fungi but 3-methyl-1-phenylpyrazol-5-one (**3**) enhanced the activity against *R. solani* with IC_{50}

value of 155 μg/ml after 4 days exposure, *P. debarianum* and *M. phaseoli* with IC_{50} values of 68 and 170 μg/ml after 6 days exposure, respectively whereas it was inactive on *F. calmorum* as its IC_{50} was >500 μg/ml. On the other hand, 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one (**4**) caused the toxic effect against *R. solani*, *F. calmorum* and *M. phaseoli* with 100, 440 and 140 μg/ml IC_{50} values, respectively after the same exposure time. From these results, some of the prepared compounds exceeded the standard fungicide in their effects against the tested fungi under the used experimental conditions.



Chemical structures of pyrazole derivatives and used standard pesticides

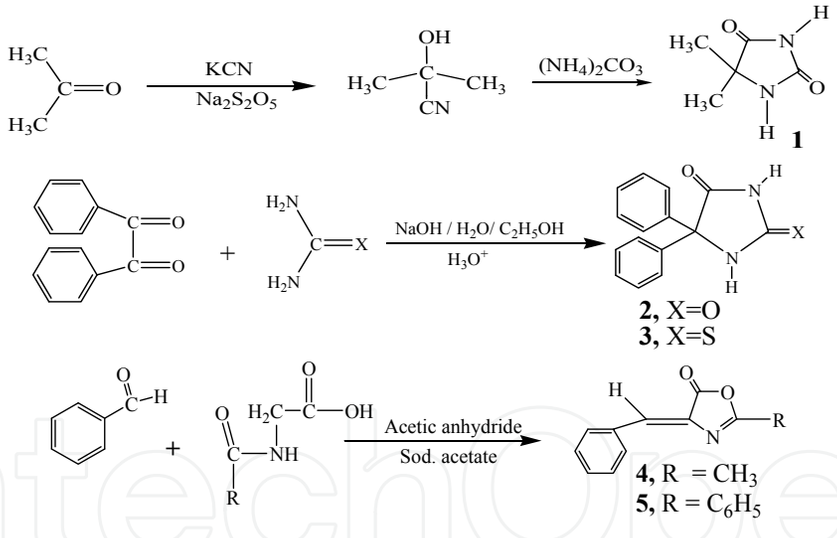
Pyrazole derivatives inhibited the growth of root and shoot systems of wheat and squash seedlings differently. Benzoylation of 3,5-dimethylpyrazole (**1**) decreased its inhibition on wheat shoot system growth, vice versa against its root system. Introducing the 2,4-dinitro- moiety enhanced the toxicity of 3-methyl-1-phenyl pyrazol-5-one (**3**) on wheat shoot and root systems. Compounds 1, 2, 3 and 4 inhibited cucumber seedlings root system with 95, 109, 95 and 58 μg/ml and its shoot system with 38, 90, 60 and 78 μg/ml, comparing with 115 and 86 μg/ml of metribuzin, respectively. It gave 81 and 52 μg/ml on wheat shoot and root systems. The standard herbicide was less effective than the tested compounds on quash shoot system. Compound **1** was inactive against *S. littoralis* (Boisid.), its activity slightly increased to 10% mortality by substitution with 1-benzoyl- moiety. The effect became 23% mortality with reduction of palatability to 8.5-50 % of control in case of phenylpyrazol-5-one in. Substitution with 2,4-dinitrophenyl- moiety decreased the activity to 14 % mortality and 50-67 % palatability.

3.4. Pesticidal effects of some imidazolidine and oxazolone derivatives [6]

Actually we were interested to evaluate pesticidal actions of some imidazolidine and oxazolone derivatives as some of them are insecticides, herbicides and fungicides [44]. So three other derivatives of imidazolidine: 5,5-dimethylimidazolidin-2,4-dione, 5,5-diphenylimidazol-idin-2,4-dione and 5,5-diphenylimidazolidin-2-thione-4-one and two oxazolone derivatives: 4-Benzylidine-2-methyloxazol-5-one and 4-Benzylidine-2-phenyl-oxazol-5-one were prepared and checked for their structure. Their fungicidal, phytocidal and insecticidal effects were carried out as in case of pyrazole derivatives.

Fungicidal activity

Imidazolidine derivatives appeared more effective than the oxazol-5-one derivatives on *R. solani* depending on the substituent on position 5. 5,5-Dimethyl moiety increased the toxicity of compound **1**, 5,5-dimethylimidazol-idin-2,4-dione than 5,5-diphenyl moiety in compound **2**, 5,5-diphenylimidazol-idin-2,4-dione with IC_{50} values of 191.8 and 447.6 µg/ml, respectively. Replacing sulfur in compound **3,** 5,5-diphenylimidazolidin-2-thione-4-one instead of oxygen at position 2 increased its toxicity with 148.4 IC_{50} value exceeding the standard fungicide (233.8 µg/ml). 2-Phenyl moiety enhanced the toxicity of compound **5**, 4-benzylidine-2-phenyl oxazol-5-one more than 2-methyl moiety in compound **4**, 4-benzylidine-2-methyl oxazol-5-one with 542.0 and 785.3 µg/ml, respectively. Vice versa against *P. debarianum*, compound **5** was the most effective among the other tested compounds with IC_{50} of 76.9 µg/ml. Imidazolidine derivatives were nearly similar or more active than standard in its effect. Compound **3** was more toxic than compounds **1**, **2**, **4** and the standard fungicide against *P. debarianum* with IC_{50} values 156.4, 357.1, 318.7, 516.5 and 334.3 µg/ml, respectively. Compounds **1** and **3** were more effective against *F. calmorum* than others with 306.7 and 314.1 µg/ml IC_{50} values. The standard fungicide exceeded all compounds against *F. calmorum*. Compound **3** was the most effective against *M. phaseoli* with 139.0 IC_{50} value surpassing all compounds including the standard fungicide.



Preparation scheme of compounds 1-5

From the obtained results, fungitoxic activities proved to be a function of both the tested compound and the used fungus. In general, through analysis of variance (ANOVA) of hyphal growth inhibition percents, compound **3,** 5,5-diphenylimidazolidin-2-thione-4-one was the most active against the tested fungi with Mean ± SE of growth inhibition equaled 34.69^{e}. The other tested compounds were arranged as Mean ± SE was 32.74 ± 2.53^{d}, 28.67 ± 2.79^{c}, 25.08 ± 2.44^{b} and 24.65 ± 2.29^{b} and 19.93 ± 2.00^{a}, respectively in case of standard fungicide, compound **5,** compounds **1** and **2**, compound **4**. *P. debarianum* was more sensitive than *R. solani, F. calmorum* and *M. phaseoli* with Mean inhibition% ± SE of 29.55 ± 2.23^{d}, 27.88 ± 2.07^{c}, 27.30 ± 1.98^{b} and 25.77 ± 2.01^{a}, respectively.

Phytocidal activity

The tested compounds inhibited germination and shoot growth of treated *T. aestivum* seeds. Compound **5** inhibited shoot growth exceeding the other prepared compounds with EC_{50} value equaled 98.6 μg/ml. Compound **2** surpassed compounds **1**, **3** and **4** with EC_{50} values equaled 154.1, 177.9, 282.6 and 703.4 μg/ml, respectively. The tested compounds inhibited germination of treated seeds with EC_{50} values ranged from 517.3 to 726.8 μg/ml. Metribuzin as a standard herbicide was the most effective inhibiting germination and shoot growth with EC_{50} values of 92.4 and 54.8 μg/ml. As a result of being these compounds more effective on seedling shoot growth than on germination process, they were tested against both the root and shoot systems of pregerminated seeds of wheat (*T. aestivum*) as a narrow leaf plant and squash (*C. pepo*) as abroad leaf plant. Compound **1** showed the lowest effect, followed by compound **4** against both the root and shoot systems of *T. aestivum*. Compound **3** exhibited the strongest effect with EC_{50} values equaled 25.2 and 35.6 μg/ml on root and shoot comparing with 53.6 and 60.6 μg/ml of the used standard herbicide. Differences in the tested compounds controlled their effect on the broad leaf plant. The standard herbicide proved to be the most active with EC_{50} values equaled 104.1 and 113.7 μg/ml and compound **5** was the next with 274.1 and 203.6 μg/ml EC_{50} values on its root and shoot systems growth. While compound **4** was less effective with 886.9 and 613.7 EC_{50} values against the root and shoot systems, the other tested compounds affected this plant with EC_{50} values ranged from 320.2 to 437.7 μg/ml.

Insecticidal activity

The tested compounds exhibited low mortality on 24 hours treated *S. littoralis* larvae. Among the studied imidazolidine derivatives, compound **2** affected it with LC_{50} value equaled 867.3 μg/ml inhibiting the feeding activity with effective concentration on 50% (EC_{50}) equaled 31.78 μg/ml. The other two derivatives caused very weak mortal effects and inhibited feeding with EC_{50} values equaled 3200 and 3489.9 μg/ml in case of compounds **1** and **3**, respectively. Regarding the oxazolone derivatives, although compound **4** exhibited mortality percent as high as 24%, it reduced the feeding with EC_{50} value equaled 376.8 μg/ml. The other oxazolone derivative (compound **5)** caused LC_{50} value equaled 659.7 μg/ml and reduced the feeding activity with EC_{50} equaled 982.5 μg/ml. So these compounds affected as antifeedants more than as killers against the studied insect and compound **2** was the most effective structure among them (Figure **5**).

The tested compounds exhibited phytocidal and fungicidal activities higher than their insecticidal effects. Differences in these compounds could be referred to chemical structure as in imidazolidine derivatives, presence of the 2-thione in compound **3** increased its fungitoxic effect nearly against all of the tested fungi. Substitution of 5,5-dimethyl moiety in compound **1** increased the toxicity more than 5,5- diphenyl moiety in compound **2** against *R. solani* and *F. calmorum* fungi. On contrary against *P. debarianum* and *M. phaseoli*, they showed almost the same effect. Their insecticidal effects were changed against the treated larvae as compound **2** exceeded the effects of the two other imidazolidine derivatives. Regarding the

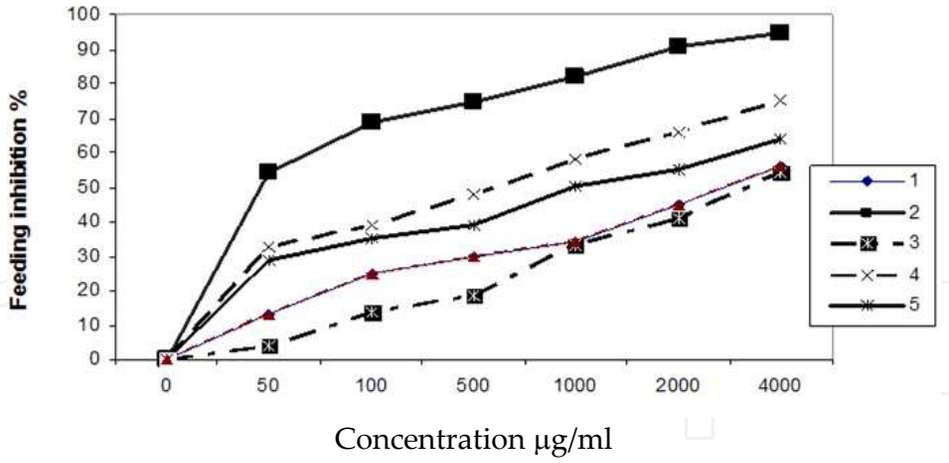


Figure 5. Feeding inhibition on *S. littoralis* Boisd. **1**, 5,5-Dimethylimidazolidin-2,4-dione**; 2,** 5,5-diphenylimidazolidin-2,4-dione; **3,** 5,5-di-phenylimidazolidin-2-thione-4-one; **4**, 4-Benzylidine-2-methyloxazol-5-one**; 5,** 4-benzyl-idine-2-phenyloxazol-5-one.

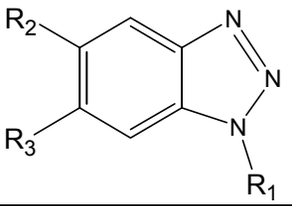
prepared oxazolones, compound **5** appeared more effective than compound **4** against the tested fungi and larvae. This difference between oxazolone derivatives could be due to the substituted moiety on C-2 position [45] as they revealed that substitution of functional group (s) at C-4 and C-2 positions plays a vital role in oxazolone series activity. They also revealed that oxazolone derivatives demonstrated excellent *in vitro* tyrosinase inhibitory. Fungitoxic effects of oxazolone derivatives maybe due to their mutagenic potential during *in vitro* DNA synthesis inducing mainly dAMP insertion [46]. The effect may referred to inhibition of fungal RNA synthetase [47]. In conclusion, compound **3**, 5,5-diphenylimidazolidin-2-thione-4-one was the most useful fungitoxic structure among the prepared compounds and so, it might be useful in controlling plant pathogenic fungi after suitable formulation and helping in integrated management programmes. It also proved to be the most suitable structure for phytotoxicity, especially for the narrow leaf weeds.

3.5. Fungicidal effects of certain benzotriazole and coumarin derivatives [48]

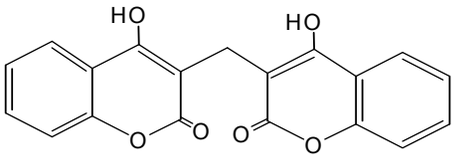
To extend the spectrum of newly discovered antifungal compounds facing continuous fungal infections, six benzotriazole derivatives as well as two coumarin derivatives were synthesized, confirmed for their structure and evaluated on *F. oxysporum*; *R. solani*; *M. phasoli*; *Helminthosporium sp* and *Alternaria alternata.* Triazole ring was chosen due to discovering some effective fungicidal triazole derivatives [49-51].

In vitro fungitoxicity effects

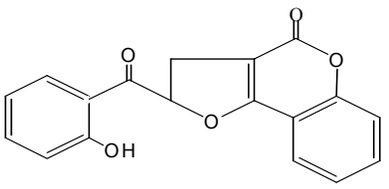
Effect of the tested 1,2,3-triazole and coumarin derivatives on three soil fungi and two foliar fungi based on their structure differences. 5,6- Dichlorobenzotriazole proved to be highly toxic against *R. solani*, *A. alternata* and *Helminthosporium sp* with IC_{50} values of 12, 20 and 27 µg/ml and moderately fungitoxic against both *M. phasoli* and *F. oxysporum* with IC_{50} values equaled 53 and 56 µg/ml. Toxicity categories are devised by [52]. However benzotriazole



Compound	R1	R2	R3
1,2,3-Benzotriazole	H	H	H
5,6-Dimethyl benzotriazole	H	CH_3	CH_3
5,6-Dichloro benzotriazole	H	Cl	Cl
1-Acetyl-5,6-dimethyl benzotriazole	CH_3CO	CH_3	CH_3
1-Benzoyl-5,6-dimethyl benzotriazole	C_6H_5CO	CH_3	CH_3
1-benzoylbenzotriazole	C_6H_5CO	H	H



3, 3 ˉ–Methelene bis –4–hydroxy coumarin, (**Dicoumarol**)



2,3–Dihydro–2-(2-hydroxybenzoyl) – 4H Furo[3,2 –C] [1] benzopyran-4- one, (**Furopyrone**)

Scheme 2. Chemical structure of tested triazole and coumarin derivatives

and 1-acetyl-5,6-dimethylbenzotriazole caused moderate effects against *M. phasoli* and *F. oxysporum* as soil fungi, respectively with equal IC_{50} values (155 μg/ml). 5,6-Dimethyl-, 1-benzoyl-5,6-dimethyl- and 1-benzoyl- benzotriazoles as well as dicoumarol and furopyrone (coumarin derivatives) needed increasing their highest concentration (200 μg/ml) to get 50% inhibition against hyphal growth of all fungi, and in case of 1,2,3-benzotriazole against *F. oxysporum* and *R. solani*; and 1-acetyl-5,6-dimethylbenzotriazole against *R. solani* and *M. phasoli*. *Helminthosporium sp* (foliar fungus) was moderately affected by 1-acetyl-5,6-dimethyl- and 1-benzoyl-5,6-dimethyl- benzotriazoles with IC_{50} values of 150 and 165 μg/ml, respectively. The other compounds could not reach 50% fungitoxicity against it at the concentration range. *A. alternata* was also moderately affected by benzotriazole; 1-benzoyl-5,6-dimethyl-; 1-acetyl-5,6-dimethyl- and 5,6-di-methylbenzotriazoles with IC_{50} values equal 150; 155; 165 and 170 μg/ml, respectively. This fungus was less sensitive to 1-benzoylbezotrtiazole and both coumarin derivatives. However, 5,6-dichloro substituent highly improved the fungitoxic effect of benzotriazole against all tested fungi, comparing with other benzotriazoles in addition to dicoumarol and furopyrone (coumarin derivatives). 1-Benzoylbenzotriazole and coumarin derivatives were less effective against all tested fungi. The weak effects of coumarin derivatives may be due to their classification as mammalian poisons. So, it could be concluded that 5,6-dichlorobenzotriazole was very good fungicide against all tested fungi. On the other hand, *A. alternata* (as a foliar fungus) was moderately affected by the other tested benzotriazoles except 1-benzoylbenzotriazole and coumarin derivatives.

In Vivo biochemical effects

a. Effect on polyphenoloxidase and peroxidase activities

5,6-Dichlorobenzotriazole at 0.1, 0.25, 0.5, 1 and 2 IC_{50} rates in μg/ml affected both polyphenoloxidase (PPO) and peroxidase (PO) enzymes for each tested fungi. Their activities were in non-systematic response depending on the type of fungus and concentration. The activity of polyphenoloxidase was highly increased in *F. oxysporum*; slightly increased in *R. solani*; weakly increased in *M. phasoli* with increasing the tested concentration; whereas, in *Helmintho-sporium sp* its activity weakly increased until 0.5 IC_{50} then weakly inhibited by IC_{50} and 2 IC_{50} rates. In case of *A. alternata* this enzyme weakly inhibited by 33.2% inhibition at 0.5 IC_{50} value, then the enzyme was slightly activated with increasing the tested rates to IC_{50} and 2 IC_{50}. Concerning peroxidase, its activity weakly increased in *F. oxysporum* at all the tested rates, weakly inhibited in *R. solani* at the lower two rates then weakly increased. In *M. phasoli* and *A. alternata*, peroxidase enzyme was highly inhibited with I_{50} values equal 39.64 and 5.78 μg/ml, respectively. 5,6-Dichlorobenzotriazole was very effective to inhibit peroxidase enzyme in *A. alternata* through all the tested rates.

b. Effect on DNA and RNA contents

5,6-Dichlorobenzotriazole at several rates of its IC_{50} values affected DNA and RNA contents in each tested fungus. In *F. oxysporum*, DNA and RNA contents as compared with control were reduced at the two lower rates (0.1 and 0.25 of IC_{50}) of 5,6-di-chlorobenzotriazole then increased with increasing the tested rates. On the other hand, their contents in *R. solani* highly increased more than control reaching the maximum peak at 0.5 IC_{50} then decreased but still more than control. DNA and RNA contents in both *M. phasolina* and *Helminthosporium sp* were decreased with increasing the tested rates of IC_{50} values. The contents in *A. alternata* were highly increased with increasing the tested rates of IC_{50} values. In conclusion, 5,6-dichlorobenzotriazole may be useful as a good fungi-cide against all the tested fungi. The 5,6-dichloro- substituent was required to improve benzotriazoles effects against all treated fungi. So, it was highly effective against the activities of polyphenoloxidase, peroxidase and DNA and RNA contents.

3.6. Rodenticidal activity of certain benzotriazole and coumarin derivatives [53]

The previously explained benzotriazole and coumarin derivatives were studied also for their rodenticidal effects against the white Noway rat. In fact the two coumarin derivatives might be expected in their effects, while the benzotriazole derivatives were tested to stand on their toxicity related to studied coumarin comparing with Coumachlor**,** 3-(α-acetonyl-4-chlorobenzyl)-4-hydroxy-coumarin as standard anticoagulant rodenticide.

During the baiting of the tested rats (*Rattus norvegicus* var. *albus*), the illness symptoms were observed as inactivity, ceasing sounds, closed eyes, bloody face, bleeding and paralysis followed by death. The internal symptoms were also observed as change the colour of liver, kidney, swelling of stomach and lungs with obvious changes, bloody bladder and intestines and the body cavity was intensively bloody. Mortality percents caused by synthesized

dicoumarol, furopyrone and 1-acetyl-5,6-dimethylbenzotriazole increased with increasing the dosages; their LD_{50} values were 64, 400 and 580 mg/kg body weight, respectively. So, both dicoumarol and furopyrone were moderately toxic, whereas 1-acetyl-5,6-dimethylbenzotriazole was slightly toxic [52]. The average times to death were ranged between 6.3 and 5.5 days. However, EP_{50} and EP_{98} (Effective periods of 50% and 98% mortalities) of 100 mg/kg were 4.5 and 11.5 days, respectively. These compounds exhibited good rodenticidal properties on three consecutive dosages in a week when compared with coumachlor with LD_{50} equal to 50-100 mg/kg if applied on five consecutive days [54].

Biochemical effects

Benzotriazole derivatives weakly affected the haemoglobin and haematocrit of both males and females within the tested doses (10-300 mg/kg) with ED_{50} of >300 mg/kg. While, dicoumarol and furopyrone were highly and moderately toxic against haemoglobin of male and female rats with ED_{50} values of 24 & 27 mg/kg and 90 & 130 mg/kg body weight, respectively. Furopyrone and dicoumarol were moderately active on haematocrit of males with ED_{50} values of 53 and 65 mg/kg but on females with 135 and 195 mg/kg respectively. Red blood cells (RBC's) of females were found to be more sensitive to coumachlor, dicoumarol, furopyrone, 5,6-dimethylbenzotriazole, benzotria-zole followed by 1-benzoyl-5,6-dimethylbenzotriazole as highly toxic compounds reducing RBC's of males with ED_{50} values of 7, 12, 19, 28, 40 and 44 mg/kg, respectively (Loomis, 1976). Coumachlor, dicoumarol, furopyrone and 5,6-dimethylbenzotriazole were also highly toxic against RBC's of females with ED_{50} value of 10.5, 25, 32 and 40 mg/kg, respectively. However the other compounds moderately reduced the RBC's counts of males and females. White blood cells (WBC's) of males were highly sensitive to 5,6- dichlorobenzotriazole, coumachlor and dicoumarol with ED_{50} values of 12, 13, and 37 mg/kg, whereas dicoumarol and 5,6-dichlorobenzotriazole were highly toxic in reducing it in females with ED_{50} values of 32 and 42 mg/kg, respectively. The other compounds proved to be moderately toxic in both males and females except benzotriazole, 1-acetylbenzotriazole and furopyrone. 5,6-Dichlorobenzotriazole was nearly equal to coumachlor in reducing males WBC's, whereas dicoumarol and 5,6-dichlorobenzotriazole were more effective than coumachlor against female WBC's.

Benzotriazole derivatives as well as furopyrone weakly affected sALT enzyme in both males and females. 5,6-Dimethylbenzotriazole was more potent reducing sAST enzyme activity in both males and females with ED_{50} values of 8.8 and 13.5 mg/kg, respectively. Dicoumarol was also highly toxic compound against sAST in males and females with ED_{50} of 24 and 32 mg/kg, respectively whereas coumachlor was highly toxic against females and moderately against males with 24 and 54 mg/kg ED_{50} values, respectively. 5,6-Dimethylbenzotriazole was more potent reducing sAST activity in both males and females with ED_{50} values of 8.8 and 13.5 mg/kg, respectively. Dicoumarol was also categorized as highly toxic against sAST in males and females with ED_{50} of 24 and 32 mg/kg, respectively whereas coumachlor was highly toxic against females and moderately against males with 24 and 54 mg/kg ED_{50} values, respectively. 1-Acetylbenzotriazole was moderate reducing sAST activity in males

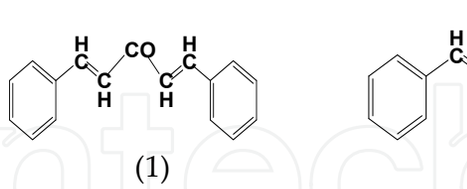
with ED_{50} equalled 160 mg/kg. The other derivatives and furopyrone weakly affected it in both sexes.

3.7. Pesticidal activity of some benzylidine derivatives [4]

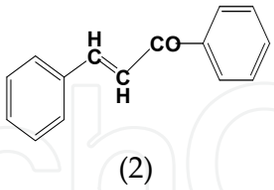
Actually α,β- unsaturated ketones were prepared according to Claisen Schmidt reaction (CSR) mechanism for searching their potency controlling some pests based on their biological history [55-56]. These biological activities of chalcone derivatives (as benzylidine derivatives) directed the attention to prepare some chaclone derivatives; dibenzylidineacetone, dibenzylidineacetylacetone and benzylidineacetophenone (chalcone).

Phytocidal Effects

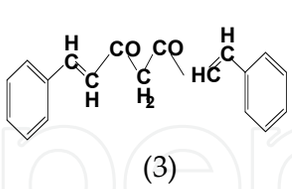
Benzylidineacetophenone (chalcone), dibenzylidineacetone and dibenzyli-dineacetylacetone were active against the root system of wheat seedlings (*Triticum aestivum*) with EC_{50} values equal 54, 55 and 68 μg/ml, respectively. On the other hand, their shoot systems were less sensitive, since benzylidineacetophenone (chalcone) was less effective, followed by dibenzylidineacetylacetone and dibenzylidine-acetone. It could be concluded that, the three prepared compounds proved to be highly toxic on root system whereas dibenzylidine acetone and dibenzylidineacetylacetone proved to be moderately toxic against the shoot system of wheat seedlings. On the other hand, root system of squash seedlings (*Cucarbita pepo*) was highly affected by dibenzylidineacetylacetone, benzylidineacetophenone and dibenz-ylidineacetone. These prepared compounds also affected the shoot system of squash seedlings. However the standard herbicide, Granstar was more effective against both wheat and squash seedlings than the prepared compounds. Although the obtained results revealed that the prepared compounds could be considered as a moderate phytotoxicants against wheat and squash seedlings but they were more specific on root system of wheat seedlings.



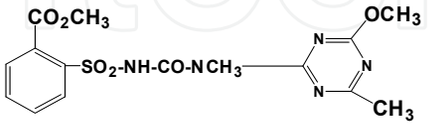
(1)



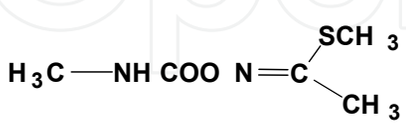
(2)



(3)



(4)



(5)

Chemical structures of the tested compounds and standard pesticides

1, dibenzylidineacetone (1,5-diphenylpenta-1,4-dien-3–one); **2**, benzylidine acetophenone (1,3-diphenyl propen-3–one) (Chalcone); **3**, dibenzylidine acetylacetone (1,7-diphenyl hepta-1,6-dien-3,5–dione); **4**, tribenuron methyl, (2-[4-methoxy-6-methyl-1,2,3-triazin-2-yl] methyl carbamoyl sulfamoyl benzoic acid) (Granstar); **5**, methomyl, S-methyl-N-(methyl carbamoyl -oxy) thioacetimidate

Insecticidal and molluscicidal effects

Comparing with methomyl (Lannate), Dibenzylidineacetone and lannate proved to be highly toxic against the cotton leaf worm (*S. littoralis*) with LC_{50} values < 10 μg/ml. Dibenzylidineacetylacetone and benzylidineacetophenone slightly affected it with LC_{50} values equalled 510 and > 2000 μg/ml, respectively. Dibenzylidineacetone weakly affected the tested snails, whereas benzylidineacetophenone was very weak against *E. Vermiculata* but it was not mortal on *T. pisana*. Dibenzylidineacetylacetone showed no lethal effects against the two terrestrial snails.

Generally, the prepared compounds caused moderately phytotoxic effects on both wheat and squash seedlings but they were specific on root system of wheat seedlings. Dibenzylidineacetone caused nearly the same effects as methomyl against cotton leaf worm. So, it could be concluded that dibenzylidineacetone after different biological tests may be safe as an insecticide against cotton leaf worm as it was previously prepared as a sun protection cream [57].

3.8. Evaluation of certain benzylidine and pyrazole derivatives against wood decay fungi [58]

Wood decay fungi are destructive agents of wood industry. They degraded the used fungicides [59,60]. Due to their importance and the activities of benzylidine and pyrazole derivatives, their toxic effects were evaluated on the white rot fungus *Coriolus versicolor* and the brown rot fungus *Gloeophyllum trabeum*.

In Vitro fungitoxic effects were dependent on their concentrations, chemical structures and the treated fungus. 1,5-Diphenylpenta-1,4-dien-3–one (compound **1)** exhibited its fungitoxicity with IC_{50} of 295.4 and 976.9 μg/ml against *C. versicolor* and *G. trabeum*, respectively. While, the toxicity was diminished because of the CH_2CO- moiety in 1,7-diphenylhepta-1,6-dien-3,5-dione (compound **2**) with IC_{50} of 317.1 and 1995.4 μg/ml in case of the two studied fungi. Fungitoxicity was more than three nine times against *C. versicolor* and *G. trabeum*, respectively without -CH=CH- moiety in 1,3-diphenylpropen-3-one (Chalcone) **(**compound **3)**. 3,5-Dimethylpyrazole **(c**ompound **4)** was less effective against the tested fungi with IC_{50} values of 867.7 and 944.8 μg/ml against *C. versicolor* and *G. trabeum*, respectively. Substitution with 1-phenyl moiety changing to pyrazol-5-one ring in 3-methyl-1-phenylpyrazol-5-one **(**compound **5)** increased the effects with IC_{50} values of 744.2 and 632.4 μg/ml against the treated fungi.. Higher enhancement was achieved by replacing the substituted 1-phenyl ring with 2,4-dinitrophenyl moiety in 3-Methyl-1-(2,4-dinitro-phenyl)-pyrazol-5-one **(**compound **6)**, the most active with IC_{50} of 19.6 and 112.7 μg/ml against the white and brown rot fungi. In general, significantly *C. versicolor* appeared more sensitive than *G. trabeum* with general mean ± SE of mycelium growth inhibition percents of 39.18 ± 3.12 and 32.7 ± 2.58, respectively. Additionally, compound **6** was the most effective followed by compound **3**, exceeding boric acid as a standard compound with mean mycelium growth inhibition percents of 61.0, 46.9 and 40.9%, respectively. While, the other tested compounds were less effective than the standard (Table **2**).

Tested Compound	*Coriolus versicolor*			*Gloeophyllum trabeum*		
	IC_{50} µg/ml (95%C L)	**Slope ± S.E**	**χ^2**	**IC_{50} µg/ml (95%C L)**	**Slope ± S.E**	**χ^2**
1,5-Diphenylpenta-1,4-dien -3–one **(1)**	**295.4** [c] (250-350)	1.51 ± 0.019	5.9	**976.9** [b] (796-1198)	1.17 ± 0.02	6.8
1,7-Diphenyl hepta-1,6-dien-3,5–dione **(2)**	**317.1** [b] (263-383)	1.35 ± 0.02	0.4	**1995.4** [a] (1452-2747)	0.93 ± 0.02	6.4
1,3-Diphenylpropen-3-one (Chalcone) **(3)**	**84.5** [e] (57.1-124.4)	0.86 ± 0.01	4.3	**103.9** [g] (66.6-160.8)	0.73 ± 0.01	2.5
3,5-Dimethylpyrazole **(4)**	**867.7** [a] (759-992)	1.96 ± 0.026	3.0	**944.8** [c] (784-1138)	1.3 ± 0.021	2.6
3-Methyl-1-phenylpyrazol-5-one **(5)**	**744.2** [b] (655-846)	2.18 ± 0.028	0.5	**632.4** [d] (549.6-728)	2.06 ± 0.026	3.9
3-Methyl-1-(2,4-dinitro-phenyl)-pyrazol-5-one **(6)**	**19.6** [f] (16.7-22.9)	2.16 ± 0.028	9.1	**112.7** [f] (88.9-142.7)	1.17 ± 0.01	3.9
Boric acid	**252.5** [d] (226-282.3)	2.38 ± 0.033	2.5	**189.1** [e] (166.3-215)	2.0 ± 0.026	7.9

Results in the same column with the same superscript are not significantly different ($p < 0.05$), DF = 4

Table 2. Fungicidal effects of certain benzylidine and pyrazole compounds on *Coriolus versicolor* and *Gloeophyllum trabeum* fungi

In vivo antifungal activity

After six weeks exposure to fungal attack, the average mass loss in control was 41.27 and 41.53% for poplar (*Populus nigra*) and Scots pine sapwood (*Pinus sylvestris*), respectively. Regarding poplar, compounds **3** and **6** reduced the mass loss to 30.43% and 29.23% (75% and 71% of control) at the lowest concentration. This effect was significantly increased reaching 23.87% (57.7% of control) and 13.67 % (33.1% of control) mass losses in systematic arrangement in un-leached samples in case of compound **3** and **6**, respectively at the highest concentration (10 IC_{50} value). Leaching reduced antifungal effects of the two compounds to 28.10 % and 28.63% mass loss at the highest concentration with a narrow range of difference with their lowest concentration (0.5 IC_{50}) as the mass loss was 33.03% and 31.13% in compound **3** and **6**, respectively. The tested compounds protected the Scots pine sapwood samples in the same manner as compound **3** reduced its mass loss to (30.83% - 24.80%) while compound **6** reduced its mass loss to (30.0% - 14.47%) at concentration used in comparison to 41.53% of control samples. Leaching of the used blocks decreased the effect to (34.87% – 29.0%) and (33.30% – 27.5%), respectively (Table **3**).

Treatment	Conc (IC_{50} values)	*Populus nigra*			*Pinus sylvestris*		
		Retention Kg/m³	Mass loss % ± SE		Retention Kg/m³	Mass loss % ± SE	
			Un-Leached	Leached		Un-Leached	Leached
Control	0.0	0.0	41.27 ^{g} ± 0.43	41.27 ^{e} ± 0.43	0.0	41.53^{g} ± 0.42	41.53^{g} ± 0.42
1,3-Diphenyl-propen-3-one Chalcone) (3)	0.5	0.022	30.43 ^{f} ± 0.77	33.03 ^{d} ± 0.37	0.021	30.83^{f} ± 0.92	34.87^{f} ± 0.37
	1.0	0.044	28.10 ^{e} ± 0.61	31.07 ^{c} ± 0.58	0.043	28.10^{e} ± 0.35	32.30^{d} ± 0.15
	5.0	0.194	26.23 ^{d} ± 0.55	29.33 ^{b} ± 0.26	0.210	26.4 ^{d} ± 0.49	31.10^{c} ± 0.51
	10.0	0.447	23.87 ^{c} ± 0.61	28.10 ^{a} ± 0.42	0.463	24.80^{c} ± 0.68	29.0 ^{b} ± 0.21
3-Methyl-1-(2,4-dinitro-phenyl) -pyr-azol-5-one (6)	0.5	0.004	29.23 ^{f} ± 0.82	31.13 ^{c} ± 0.52	0.019	30.0 ^{f} ± 0.32	33.30^{e} ± 0.38
	1.0	0.009	23.40 ^{c} ± 0.67	30.13 ^{c} ± 0.55	0.039	25.57^{d} ± 0.43	31.17^{c} ± 0.15
	5.0	0.042	18.07 ^{b} ± 0.45	29.40 ^{b} ± 0.35	0.199	20.87^{b} ± 0.20	29.47^{b} ± 0.55
	10.0	0.089	13.67 ^{a} ± 0.54	28.63 ^{b} ± 0.37	0.394	14.47^{a} ± 0.34	27.5 ^{a} ± 0.58

Results in the same column with the same superscript are not significantly different ($p < 0.05$).

Table 3. Average of retention (kg/m3) and mass losses (%) of Poplar (*P. nigra)* and Scots pine sapwood (*P. sylvestris*) mini-blocks treated with compounds 3 and 6 and exposed to *C. versicolor* and *G. trabeum*, respectively.

The effect of compound **6 was reduced by leaching** samples more than compound **3** ensuring that the former is easily leached due to its hygroscopic nature. Descriptive analysis proved compound **6** more significantly effective with general mean of mass loss ± SE of 25.12% ± 2.58 in comparison to 29.98% ± 1.63 of compound **3** in case of un-leached poplar samples, while no significant differences between them in leached samples were observed. In Scots pine sapwood, significance appeared in both cases as compound **6** achieved general mean of mass loss ± SE of 26.49% ± 2.44 and 32.59% ± 1.31 comparing with 30.33 % ± 1.61 and 33.76 % ± 1.16 of compound **3** in un-leached and leached samples. Differences between the benzylidine derivatives in their fungicidal activity could be referred to the conjugation among carbonyl groups, phenyl rings and double bonds, so compound **2** was less effective due to lack of this conjugation because of CH_2 moiety. Compound **3** was more effective than compound **1** may be due to the lipophilicity [61]. The effect of benzylidine derivatives (benzaldhyde derived compounds) was greatly inhibited against *G. trabeum* than *C. versicolor*, which may be due to degradation as benzaldehyde and its metabolic intermediates were effectively degraded by *G. trabeum* to 3,4-dihydroxybenzoic acid. This was further metabolized via the decarboxylation reaction to yield 1,2,4-trihydroxybenzene, which is susceptible to the ring-fission reaction [62]. Compound **3** was retained approximately in the same amount in both wood specimens. The retained amount of compound **6** in *P. sylvestris* was four times more than in *P. nigra*. On the other hand, compound **6** was retained in about one fifth of compound **3** in *P. nigra*, although it was more effective. So it could be concluded that compound **6** was found to be more effective than compound **3** in all cases and it was more toxic against *C. versicolor* than on *G. trabeum*. Moreover, these compounds need to be applied at higher concentrations to enter wood preservatives clique.

3.9. Phytocidal effects of some azole derivatives [63]

Phytocidal effects of five-memberred heterocyclic derivatives were studied on monocotyledonous (*Triticum aestivum* L.) and dicotyledonous (*Cucurbita pepo*) plants. Some activities of nitrogen heterocycles as herbicides [64-65] helped growing this idea.

In seed treatment, wheat seedlings growth was more sensitive to the tested compounds than seed germination. Pyrazole derivatives were less effective than both indole and benzotriazole derivatives against seed germination, while their effects against vegetation depended on the structure. 5,6-Dichlorolbenzotriazole was more potent than the standard herbicide, metribuzin against both seed germination and growth of seedlings. 1-Acetylindole-3-butyric acid caused nearly the same effect of metribuzin on seed germination, whereas its effect on seedling growth was less than it. However, the other benzotriazole, indole and pyrazole derivatives were less effective than it against both seed germination and seedling growth. Screening effects of the tested compounds on root and shoot systems of squash (*C. peppo*) and wheat (*T. aestivum*) proved 5,6-dichlorolbenzoriazole the most effective inhibiting squash root and shoot systems with EC_{50} values equaled 8.6 and 16.8 μg/ml exceeding the standard herbicides with 86.2 and 97.2 μg/ml, respectively. 1-Acetyl-5,6-dimethylbenzotriazole and 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one were also more potent than metribuzin, with EC_{50} values equaled (26.2 and 47.2) and (72.2 and 77.1) μg/ml against root and shoot systems of squash seedlings. 5,6-Dimethylbenzotriazole, 1-benzoylbenzotriazole and 1-acetylindole-3-butyric acid were more effective than it against squash root system with 63.1, 71.2, and 80.1 μg/ml EC_{50} values. Indole-3-butyric acid inhibited squash shoot system with EC_{50} value equaled 63.7 μg/ml. The other tested benzotriazoles, indole and pyrazole derivatives were less effective than the standard herbicide. Comparing with 55.8 and 68.2 μg/ml EC_{50} values of the standard herbicide against root and shoot systems of wheat, 5,6-dichlorolbenzotriazole, indole-3-butyric acid, indole-3-acetic acid, 1-acetylindole-3-butyric acid, benzotriazole, 1-benzoylindole-3-acetic acid and 3-methyl-1(2,4-dinitrophenyl)pyrazol-5-one were more potent with 16.9, 6.0, 3.3, 2.86, 1.82, 1.8 and 1.45 times against root system of wheat. While 5,6-dichlorolbenzotriazole was 5.3 times more effective than metribuzin on wheat seedlings shoot growth, the other benzotriazoles, indole and pyrazole derivatives were less effective than it. All the tested derivatives were more effective inhibiting growth of root system than shoot growth in squash (*C. peppo*) seedlings except indole-3-acetic acid with EC_{50} values equaled 311.4 and 201.4 μg/ml and 3-methyl-1-(2,4-dinitrophenyl) pyrazol-5-one with EC_{50} values equaled 47.2 and 77.1 μg/ml. The same trend was obtained in case of wheat seedlings by benzotriazole and indole derivatives except 1-benzoylindole-3-butyric acid with EC_{50} values equaled 611 and 544 μg/ml and 1-benzoyl-2-phenylindole with EC_{50} values equaled 453 and 503 μg/ml, respectively. However pyrazole derivatives proved to be more effective against root than shoot depending inhibition degree on the chemical structure differences among the applied derivatives except 3,5-dimethylpyrazole with EC_{50} values equaled 208 and 172 μg/ml, respectively. Due to high effects of both 5,6-dichlorobenzotriazole and 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one, they were applied in post emergence treatment to study their effects against some plant active sites of action. Pre emergence treatment with 5,6-

dichlorobenzotriazole inhibited both fresh and dry weights of wheat seedlings. Fresh weight of the emerged wheat seedlings was reduced with 45.1 - 94.7% at a concentration of 2 - 30 µg/ml with EC_{50} values equaled 2.9 µg/ml, while their dry weight was reduced increasingly with increasing the concentration with 30.6 - 94.2% reduction with EC_{50} value equaled 3.6 µg/ml. At 50 µg/ml, it completely prevented seeds emergence. Post-emergence treatment of wheat seedlings with 5,6-dichlorobenzotriazole and 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one affected their dry weight increase depending on concentration and time after treatment. Both two compounds reduced this increasing rate in comparison to control at all times. The highest effect was obtained during the first three days after treatment at all concentrations. 3-Methyl-1-(2,4-dinitrophenyl)pyrazol-5-one highly affected it during seven days after treatment. It was more potent than 5,6-dichlorobenzotriazole nearly at all the tested concentrations (Figure **6**).

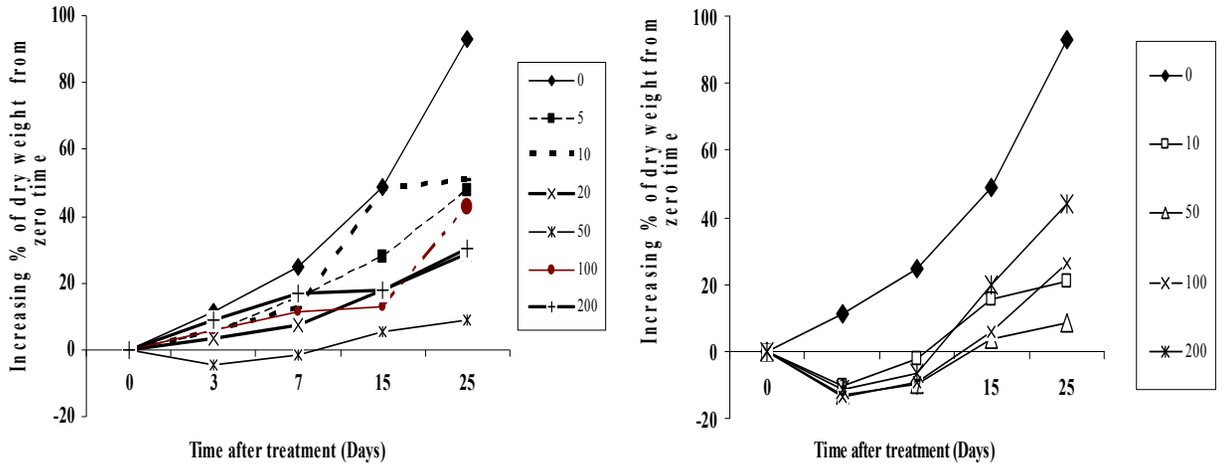


Figure 6. Effect of post emergence treatment on wheat seedlings dry weight.
Left, 5,6-dichlorobenzotriazole; **Right**, 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one

Concentrations in µg/ml

Single post-emergence treatment with both 5,6-dichlorobenzotriazole and 3-methyl-1-(2,4-dinitro-phenyl)pyrazol-5-one affected the total soluble sugars contents in a function of concentration and time after treatment (Figure **7**). Both reduced and non-reduced sugars alternatively changed regarding the time after treatment. 100 μg/ml was the most effective concentration reducing TSS increasingly with time after treatment. Low activity at 200 μg/ml might be referred to its difficult penetration. However 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one showed its maximum activity after 7 days at 100 μg/ml. The highest effect of 5,6-dichlorobenzotriazole on chlorophyll was after 3 days. At 15 days after treatment, chlorophyll contents were enhanced at all concentrations. Chlorophyll **a** was more sensitive than **b** Vice versa, 3-methyl-1-(2,4-dinitrophenyl)pyr-azol-5-one affected chlorophyll **a** less than **b.** Enhancement was noticed at low concentrations at all the tested periods. The most reducing concentration was 100 µg/ml. Treatment with 5,6-dichlorobenzotriazole reduced the soluble phenolics content mostly until 3 days after treatment at all concentrations systematically with increasing the tested concentration. This effect was fluctuated

according to the applied concentration at 7 days after treatment. The most effective concentration was 100 μg/ml. At 15 days after treatment, it was too long to keep its effectiveness in reducing their content. While 3-methyl-1-(2,4-dinitrophenyl) pyrazol-5-one caused reduction of their content up to 15 days after treatment. Effects on chlorophyll content disturb several physiological processes in plants. The effect on soluble phenolics interferes in the protective compounds [66]. Fluctuated results of chlorophyll and soluble phenolics may be due to the interactive effects of temperature and the accumulated soluble phenolics [67]. 5,6-dichlorobenzotriazole may inhibit cell division and protoporphyrinogen oxidase leading to membrane disruption and inhibiting photosynthesis [64]. Benzotriazoles are effective in blocking photosynthetic electron transfer [68], slowing down the growth and decreasing plant size emphasizing our results on fresh and dry weight [69]. They may affect through inhibition of protein kinases [70]. Indole derivatives effects varied based on structure and concentrations inducing growth abnormalities leading to desiccation, tissue necrosis, and decay. They also increased H_2O_2 levels, which contributes to the induction of cell death, deoxyribonuclease (DNase) activity and chlorophyll loss as sensitive indicators for tissue damage [65]. Pyrazole derivatives are considered as branched chain amino acid synthesis (ALS or AHAS) inhibitor stopping cell division and plant growth.

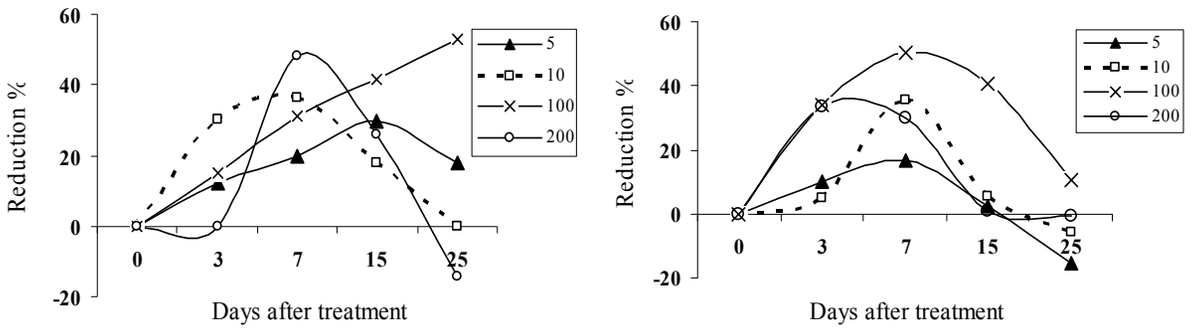


Figure 7. Effect of post emergence treatment on wheat seedlings sugars. **Left**, 5,6-dichlorobenzotriazole; **Right**, 3-methyl-1-(2,4-dinitro-phenyl) pyrazol-5-one; Concentrations in μg/ml

4. Conclusion

Several prepared organic compounds are tested for their pesticidal actions. Indole derivatives inhibited hyphal growth of several plant pathogenic fungi based on treated fungus and structure affecting sugars, RNA and DNA contents as well as enzymes disturbing cell physiology. They caused lethality, larval weight reduction, inhibition of pupation and adult emergence with inhibiting egg hatchability of *S. littoralis* Boisd. Tested pyrazole, imidazole and oxazole derivatives exhibited weak lethality with inhibition of insect palatability and moderate to high fungitoxic and phytotoxic effects according to structure, fungus and plant seedlings. Imidazolidine and oxazolone derivatives were antifeedants more than killers against *S. littoralis* and 5,5-diphenylimidazol-idin-2,4-dione was the most effective structure. Their phytocidal and fungicidal activities were higher than insecticidal effects and 5,5-diphenylimidazolidin-2-thione-4-one was the most useful structure. Benzotriazoles changed in their fungicidal effects and 5,6-dichlorobenzotriazole was highly to moderately toxic against the treated fungi affecting both polyphenoloxidase, peroxidase and DNA & RNA contents. They caused lower effects on hae-

moglobin and haematocrit of rats, whereas dicoumarol and furopyrone highly reduced them. However dimethyl- and dichloro- substituent increased the activity of non-substituted benzotriazole on RBC's, WBC's and sAST, aceylation of 5,6-dimethylbenzotriazole decreased its effect on both male and female RBC's, sAST. Benzylidine derivatives caused moderately phytotoxic effects. Dibenzylidineacetone caused nearly the same effect as methomyl against cotton leaf worm. They differed in their mortality on *E. vermiculata* and *T. pisana* snails. Significantly *C. versicolor* was more sensitive than *G. trabeum* to benzylidine and pyrazole derivatives. 3-Methyl-1-(2,4-dinitro-phenyl)-pyrazol-5-one was the most effective followed by 1,3-diphenylpropen-3-one, exceeding boric acid, as a standard in case of un-leached poplar samples, while no differences were observed between them in leached samples. In Scots pine sapwood, significance appeared in both samples. 1,3-Diphenylpropen-3-one was approximately retained in the same amount in both wood specimens. Although 3-methyl-1-(2,4-dinitrophenyl)-pyrazol-5-one was retained in one fifth of 1,3-diphenylpropen-3-one in *P. nigra*, it was more effective. Benzotriazole, indole and pyrazole derivatives inhibited wheat seedlings growth more than seed germination process. Pyrazoles were less than others inhibiting seed germination, effects on vegetation depended on structure. Some of derivatives exceeded the standard herbicides in their effects. 5,6-dichlorolbenzoriazole was the most effective inhibiting monocotyledons and dicotyledonous seedlings growth. Its pre emergence treatment inhibited wheat seedlings fresh and dry weights. They also affected the total soluble sugars, chlorophyll and soluble phenolic contents in plants. The configuration of 5,6-dichlorolbenzotriazole and 5,6-dichloro- substituent may be required to get good results. These results may exhibit 5,6-dichlorobenzotriazole as pre-emergent phytocidal compound, while 3-methyl-1-(2,4-dinitrophenyl)pyrazol-5-one as post-emergent. These results proveed 5,6-dichlorobenzotriazole to inhibit the chlorophyll content, cell division leading to membrane disruption, inhibiting photosynthesis, growth abnormalities leading to desiccation, tissue necrosis and decay and decrease the plant size emphasizing our obtained results on fresh and dry weight. In conclusion, this research might help finding active molecules are not famous as pesticides to be useful in integrated management programs.

Author details

Ahmed S. Abdel-Aty
Department of Pesticide Chemistry &Technology, Faculty of Agriculture, El-Shatby, Alexandria University, Alexandria, Egypt

5. References

[1] Benson F R, Hartizel LW, Savell WL(1952) 5,6-Dimethyl benzotriazole and its acyl derivatives. J. Am. Chem. Soc. 74: 4719.

[2] Vogel A I (1976) A text book of practical organic chemistry 4th edition. BNNO 582443946 Thames Polytechnic London, S.E. 16 6PF 886p.

[3] Abdel-Aty A S (1996) Rodenticidal activity of certain organic molecules "Chemistry and rodenticidal activity of some benzotriazole and coumarin derivatives". MSc, Pesticide Chem. Department, Faculty of Agriculture, Alexandria University, Egypt.

[4] Abdel-Aty A S (2004) Pesticidal effects of some benzylidine derivatives. Alex. J. of Agricultural Res. 49 (1): 99- 105.

[5] Abdel-Aty A S (2007) Pesticidal activities of some pyrazole derivatives. J. Adv. Agric. Res. 12 (4): 783-793.

[6] Abdel-Aty A S (2009) Pesticidal activity of some imidazole and oxazole derivatives. World J. of Agricultural Sci. 5 (1): 105-113.

[7] Abdel-Aty A S (2010) Fungicidal activity of certain indole derivatives against some plant pathogenic fungi. J. Pestic. Sci. 35 (4), 431–440.

[8] Torgeson D C (1967) Fungicides. vol.1, Agricltural and industerial applications environmental interactions. Academic Press New York and London

[9] El Ghaouth E A, Arul J, Grenier, Asselin A (1992) Antifungal activity of chitosan on two postharvest pathogens of strawberry fruits. Phytopathol., 82: 398-402.

[10] Topps J H, Wain RL (1957) Investigation on fungicides. III. The fungitoxicity of 1- and 5-alkyl salicylanilide and p-chloroanilines. Ann. Appl. Biol., 45 (3): 506-511.

[11] Finney D J (1971) Probit analysis. 3rd edition Cambridge University Press, London 38p.

[12] Broesch S (1954) Colorimetric assay of phenol oxidase. Bull. Soc. Chem. Biol. 36: 711-713.

[13] Fehrmaun H, Dimond AE (1967) Peroxidase activity and phytophthora resistance in different organs of potato plant. Phytopathol. 57: 69-72.

[14] Stoev E A, Makarova VG (1989) Laboratory manual in biochemistry. Mir Publishers, Moscow; p.66-71.

[15] Lowry OH, Rosebrough NJ, Farr AL, Randall RJ (1951) Protein measurements with folin phenol reagent. J. Biol. Chem., 193: 265- 275.

[16] Hegazi E M, El-Menshawy A M, Hammad SM (1977) Mass rearing of the Egyptian cotton leafworm, *Spodoptera littoralis* (Boisd.) on semi-artificial diet. Proc.2nd Arab Pesticide Conf., Tanta Univ. pp. 61–70.

[17] Kubo I, Nakanishi K (1977) In "Host plant resistance to pests." Hedin. P. A. Ed., American Chemical Society: Washington, ACS Symp. Ser. No. 62, P.165.

[18] Grodzinsky A M, Grodzinsky DM (1973) Short reference in plant physiology. Naukova Domka, Rev, R. U.S.: 433-34.

[19] Zemanek J(1963) The method of testing the effectiveness of herbicides on agar medium Rostle. Vyroba 9: 621- 632.

[20] Thomas W, Dutcher R A (1924) Picric acid method for Carbohydrate. J. Am. Chem. Soc. 46: 1662-1669.

[21] Hipkins M F, Baker NR (1986) Photosynthesis energy transduction. Spectroscopy, IRL Press, Oxford, Washington: 51-101

[22] McCue P, Zhheng Z, Pinkham JL, Shetty K (2000) A model for enhanced pea seedling vigour following low pH and salycilic acid treatments. Process Biochem. 35: 603-613.

[23] Horii A, McCue P, Shetty K (2007) Seed vigour studies in corn, soybean and tomato in response to fish protein hydrolysates and consequences on phenolic-linked responses. Bioresource Technol. 98: 2170-2177.

[24] Desheesh M A, El-doksch HA, El-Sebaii M A, Kadous E A, Abdel-Aty A S (1997) Isolation, identification and biological activities of several organic compounds from families Chenobodiaceae and Plumbaginaceae weeds. Alex. Sci. Exch. 18 (4): 439-447.

[25] Wintrobe MM (1965) Clinical hematology, 4th ed. Lea & Febiger philadelphia.
[26] Dacie J V, Lewis S M (1991) Practical hematology, 7th ed. 624p.
[27] Reitman S, Frankel S (1957) Acoduimetric method for the determination of serum glutamic oxaloacetate and glutamic pyruvate trans aminase. Am. J. Clin Path. 28:56.
[28] Yu T, Zheng X D (2007) Indole-3-acetic acid enhances the biocontrol of *Penicillium expansum* and *Botrytis cinerea* on pear fruit by *Cryptococcus laurentii*. FEMS Yeast Res. 7 (3): 459-64.
[29] Slininger P J, Burkhead K D, Schisler DA (2004) Antifungal and sprout regulatory bioactivities of phenylacetic acid, indole-3-acetic acid, and tyrosol isolated from the potato dry rot suppressive bacterium *Enterobacter cloacae* S11:T:07. J Ind Microbiol Biotechnol. 31 (11): 517-24.
[30] Wang H X, Ng T B (2002) Demonstration of antifungal and anti-human immunodeficiency virus reverse transcriptase activities of 6-methoxy-2-benzoxazolinone and antibacterial activity of the pineal indole 5-methoxyindole-3-acetic acid. Comp Biochem. Physiol. C Toxicol. Pharmacol. 132 (2): 261-268.
[31] Ryu C K, Lee J Y, Park R E, Ma M Y, Nho J H (2007) Synthesis and antifungal activity of 1H-indole-4,7-diones. Bioorg. Med. Chem. Lett. 17 (1): 127-131.
[32] Sharaf E F, Farrag A A (2004) Induced resistance in tomato plants by IAA against *Fusarium oxysporum lycopersici*. Pol. J. Microbiol. 53 (2): 111-116.
[33] Kumar V, Kumar A, Kharwar R N (2007) Antagonistic potential of fluorescent pseudomonads and control of charcoal rot of chickpea caused by *Macrophomina phaseolina*. J Environ Biol. 28 (1): 15-20.
[34] Folkes L K, wardman P (2001) Oxidative activation of indole-3-acetic acid to cytotoxic species a potential new role for plant auxins in cancer therapy. Biochem. Pharmacol. 61: 129–136.
[35] Kappas A (1983) Genotoxic activity of plant growth-regulating hormones in *Aspergillus nidulans*. *Carcinogenesis* 4 (11): 1409-11.
[36] Ali S E, Abdel-Aty A S (2010) Insecticidal activity of some indole derivatives. against *Spodoptera littoralis* (Boisd.). Alex. J. Agric. Res. 55 (1): 1 - 11.
[37] Ben Jannet H, Harzallah-Skhiri F, Mighri Z, Simmonds M S, Blaney W M (2000) Responses of *Spodoptera littoralis* larvae to Tunisian plant extracts and to neo-clerodane diterpenoids isolated from *Ajuga pseudoiva* leaves. Fitoterapia 71 (2): 105–112.
[38] Glazebrook J (2005) Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens. Annu. Rev. Phytopathol. 43: 205–227.
[39] Gigolashvili T, Berger B, Mock H P, Muller C, Weisshaar B, Flugge U I (2007) The transcription factor HIG1/MYB51 regulates indlic glucosinolate biosynthesis in *Arabidopis thaliana.* Plant J. 50: 886–901.
[40] Bodur E, Cokugras A N (2005) The effects of indole-3-acetic acid on human and horse serum butyryl cholinesterase. Extended Abstracts/Chemico-Biological Interactions 157-158: 373–377.
[41] De Melo M P, Pithon-Curi T C, Curi R (2004) Indole-3-acetic acid increases glutamine utilization by high peroxidase activity-presenting leukocytes. Life Sci. 75 (14): 1713–1725.

[42] Olgen S, Kiliç Z, Ada A O, Coban T (2007) Synthesis and evaluation of novel N-H and N-substituted indole-2- and 3-carboxamide derivatives as antioxidants agents. J Enzyme Inhib Med Chem. 22 (4): 457–462.

[43] Kocyi B, Kayamacio L, Rollas S (2002) Synthesis, characterization and evaluation of antituberculosis activity of some hydrazones. Farmaco 57(7): 595-599.

[44] Fidanza M A, Dernoeden P H (1996) Brown patch in perennial ryegrass as influenced by irrigation, fungicide, and fertilizers. Crop Sci., 36 (6): 1631-1638.

[45] Khan K M, Mughal U R, Khan M T, Zia U, Perveen S, Choudhary M I (2006) Oxazolones: new tyrosinase inhibitors; synthesis and their structure-activity relationships. Bioorg. and Medicin. Chem. 14 (17): 6027-6033.

[46] Duarte V, Gasparutto D, Jaquinod M, Cadet J (2000) In vitro DNA synthesis opposite oxazolone and repair of this DNA damage using modified oligonucleotides. Nucleic Acids Res. 28 (7): 1555-63.

[47] Tandon M, Coffen D L, Gallant P, Keith D, Ashwell M A (2004) Potent and selective inhibitors of bacterial methionyl tRNA synthetase derived from an oxazolone-dipeptide scaffold. Bioorg. and Medicin. Chem. Lett. 14 (8): 1909-11.

[48] Ahmed S M, Abdel-Aty A S, Desheesh M A (2004) Fungicidal effects of certain benzotriazole and coumarin derivatives. Alex. Sci. Exch. 25 (2): 321-330

[49] Holla B S, Poojary K N, Balakrishna K, Gowda P V, Kalluraya B (1996). Synthesis, charaterization and antifungal activity of some N-bridged heterocycles derived from3-(3-bromo-4-methoxyphenyl)-4-amino-5-mercapto1,2,4 triazole. Farmaco Edizione scientifica 51 (12): 793-99.

[50] Yoo B R, Suk M Y, Han J S, Mu Y M, Hong S G, Jung I (1998) Synthesis and biological evaluation of [1-(1H-1,2,4-triazol-1-yl) alkyl]-1-silacyclopentanes. Pesticide Sci. 52 (2): 138-144.

[51] Sheng X L, Jin X L, Yang F, Zheng G (1999) Study on the techniques of chemical control on wheat root disease. Acta Phytophylacica Sinica 26 (1): 69-73.

[52] Loomis T A (1976) *Essentials of Toxicology.* 2nd ed. Lea & Febiger, Philadelphia.

[53] Desheesh M A, El- Shazly A M, Kadous E A, Abdel-Aty A S (2002) Biochemical and rodenticidal activities of some synthesized 1,2,3-triaz-ole and coumarin derivatives on albino rat (*Rattus norvgicus* var. *albus*). Proc. 1st Conf. of the Central Agric. Pesticide Lab. Sep. 2002, I: 295- 305.

[54] Brooks J E, Rowe F P (1974) Commensal rodent control. WHO/ VBC/79. 726.

[55] Friis-Moller A, Fuursted C M, Christensen K SB, Kharazmi A (2002) *In vitro* antimycobacterial and antigionella activity of licochalcone A from Chinese licorice roots. Planta Med. 68 (5): 416-419.

[56] Gonzalez J J, Estevez B A (1998) Effect of (E)-chalcone on cyst nematodes (*Golobodera pallida* and *G. rostochinensis)*. J. Agric. and Food Chemistry 46 (3): 1163-1165.

[57] Conrad D. (1933)Organic Syn, 12: 22. (In Windholz, M.; S. Budavari; R. Blumetti and E. Otterbein (eds) (1983). An encyclopedia of chemicals, drugs and biologicals. Merck & Co., INC. Rahway, NS., USA: 2977)

[58] Abdel-Aty A S, Mohareb A S O (2008) Preliminary evaluation of certain benzylidine and pyrazole derivatives against wood decay fungi. Journal of Pest Cont. and Environ. Sci. 16 (2): 111-125.

[59] Kramer C, Kreisel G, Fahr K, Kässbohrer J, Schlosser D (2004) Degradation of 2-fluorophenol by the brown-rot fungus *Gloeophyllum striatum*: evidence for the involvement of extracellular Fenton chemistry. Appl Microbiol Biotechnol. 64 (3): 387-395.

[60] Mares D, Romagnoli C, Andreotti E, Forlani G, Guccione S Vicentini C B (2006) Emerging antifungal azoles and effects on *Magnaporthe grisea*. Mycol. Res. 110 (6): 686-96.

[61] Cheng S S, Liu J Y, Hsui Y R, Chang S T (2006) Chemical polymorphism and antifungal activity of essential oils from leaves of different provenances of indigenous cinnamon (*Cinnamomum osmophloeum*). Bioresour Technol. 97 (2): 306-12.

[62] Kamada F, Abe S, Hiratsuka N, Wariishi H, Tanaka H (2002) Mineralization of aromatic compounds by brown-rot basidiomycetes - mechanisms involved in initial attack on the aromatic ring. Microbiology 148 (Pt 6): 1939-46.

[63] Abdel-Aty A S (2011) Phytocidal effects of some azole derivatives. J. of Pest Cont. and Environ. Sci., 19 (1): 15-37.

[64] Luo Y P, Jiang L L, Wang G D, Chen Q, Yang G F (2008) Synthesis and herbicidal activities of novel triazolinone derivatives. J Agric. Food. Chem. 56 (6):2118-24.

[65] Grossmann K (2003) Mediation of herbicide effects by hormone interactions J. Plant Growth Regulat. 2: 109–122

[66] Ruhland C T, Fogal M J, Buyarski C R, Krna M A (2007) Solar ultraviolet-B radiation increases phenolic content and ferric reducing antioxidant power in Avena sativa. Molecules 12 (6): 1220-1232.

[67] Oncel I, Keleş Y, Ustün A S (2000) Interactive effects of temperature and heavy metal stress on the growth and some biochemical compounds in wheat seedlings. Environ Pollut. 107 (3): 315-320.

[68] Sung N D, Park H J, Park S H, Pyon J Y (1991) Herbicidal activity and molecular design of benzotriazole derivatives. J. Korean Agric. Chem. Soc. 34 (3): 287-294.

[69] Beek J R (1987) Plant Growth Regulating Triazoles [P]. EP 0227284 A1, 1987-01-07.

[70] Szyszka R, Grankowski N, Felczak K, Shugar D (1995) Halogenated benzimidazol-es and bezotriazoles as selective inhibitors of protein kinases CKI and CKII from *Saccharomyces cerevisiae* and other sources. Biochem. and biophys.l Res. Comm. 208 (1): 418-424.